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SYDNEY, SATURDAY, MAY 29, 1943.

No. 22.

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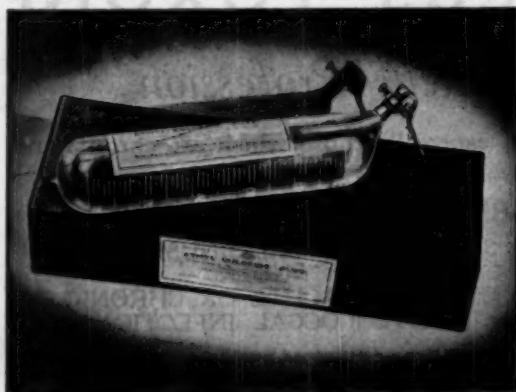
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# THE MEDICAL JOURNAL OF AUSTRALIA

VOL. I.—30TH YEAR.

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No. 22.

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### SUPPLEMENT NUMBER 16 ON WAR MEDICINE AND SURGERY: War Injuries of the Eye.

#### THE HIPPURIC ACID TEST IN THYREOTOXICOSIS.

By HUGH R. G. POATE,  
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THE conjugation of glycine and benzoic acid to form hippuric acid is a normal metabolic process probably common to all mammals. It is quantitatively more important in herbivorous animals because of the presence in vegetable materials of relatively large amounts of substances such as quinic acid<sup>(1)</sup> capable of giving rise to benzoic acid when ingested by animals. As an alternative means of detoxication benzoic acid is also conjugated with glycuronic acid, and the proportion of hippuric acid and 1-benzoylglycuronic acid<sup>(2)</sup> formed varies with the quantity of benzoic acid ingested and the species of animal examined. There is also considerable specific variation in the site of conjugation of the benzoic acid and glycine. In the dog, which detoxicates benzoic acid chiefly as 1-benzoylglycuronic acid,<sup>(3)</sup> the kidney is the only organ capable of synthesizing significant amounts of hippuric acid. In the rabbit, however, the liver is probably the chief, if not the only site of synthesis.<sup>(4)</sup> It seems probable that in man also, the synthesis of hippuric acid is confined to the liver, and it has been shown that not more than about 5% of ingested benzoic acid is conjugated with glycuronic acid.<sup>(5)</sup> These differences gave rise to considerable confusion, and although the use of benzoic acid in a

test of hepatic function had been suggested some years previously,<sup>(6)</sup> it did not receive extensive trial until after Quick described his technique.

In describing the test for clinical use, Quick<sup>(6)</sup> proposed the use of an oral dose of 5.9 grammes of sodium benzoate (the equivalent of 5.0 grammes of benzoic acid), the collection of four specimens of urine at intervals of one hour, and the determination of the amount of hippuric acid in each of these either by the "simple clinical method" or by formol titration after extraction of the hippuric acid with ether in a continuous extraction apparatus. Quick's criteria of a normal response were the following: an excretion of 1.0 gramme or more in the second and third hours, and a total excretion in the four hours of not less than 3.0 grammes (the values being in terms of benzoic acid). The subject's four-hour total is expressed as a "percentage normal" (3.0 grammes being "100% normal"), and any result above "85% normal" is considered within the normal range.

There are several objections to this test in its original form. The analytical method lacks accuracy and precision, and in many cases the large dose of sodium benzoate gives rise to nausea and often vomiting. For hospital use the four-hour test period may be inconveniently long, and the need for four analyses in each test places a heavy additional burden on a busy clinical laboratory. The relation of renal function to the test has also received attention,<sup>(7)</sup> as have dehydration, vomiting, gastric stasis and diarrhoea.

Quick, Ottenstein and Weltchek have eliminated some of these objections in the recently described<sup>(8)</sup> "intravenous" modification of the test, which occupies only one hour. The inaccuracy of the analytical method lies chiefly in the "solubility correction", which purports to allow for the hippuric acid remaining in solution after the addition of mineral acid. The correction used by Quick<sup>(6,9)</sup> is equivalent to 0.33 gramme of hippuric acid per 100 millilitres, which is the solubility of hippuric acid in water at 20° C.<sup>(10)</sup> The presence of mineral acid tends to reduce this solubility; but the presence of other substances may either increase or decrease it. Quastel and Wales<sup>(11)</sup> hold that 0.45 gramme per 100 millilitres more nearly represents

<sup>1</sup> Work done during tenure of the Senior Fellowship in Surgery, Prince Henry Hospital, Sydney. Acknowledgement is made to the Deputy Director of Medical Services, New South Wales Lines of Communication Area, for permission to contribute to this article.



the average solubility in the acid-urine mixture, and we have occasionally encountered specimens of urine known to contain 0.8 grammes of hippuric acid per 100 millilitres which failed to give a precipitate under the conditions described by Quick. Weichselbaum and Probst<sup>(12)</sup> have shown that the addition of large quantities of sodium chloride reduces the magnitude and range of variation of this correction. Other salts behave similarly.<sup>(13)</sup>

Probst<sup>(14)</sup> and Londe,<sup>(15)</sup> using this modification of the analytical method, in a group of fourteen normal subjects obtained an average four-hour excretion total equivalent to 3.7 grammes of benzoic acid. This increase on Quick's 3.0 grammes average they attributed almost entirely to the improved analytical technique. These authors also concluded that 4.0 grammes (but not 3.0 grammes) of sodium benzoate were sufficient to elicit maximal response from the liver (maximal response meaning maximal excretion in any one of the four hours after the test dose had been given). Nausea occurs less frequently after the four-gramme dose, vomiting rarely. In a later paper Londe and Probst<sup>(16)</sup> gave data on the dosage suitable for children. Probst<sup>(17)</sup> and Londe calculated all their results in terms of sodium benzoate; they considered the excretion of 50% of the test dose within two hours and 80% within four hours to be the lowest normal values.

In spite of its shortcomings, the hippuric acid test has been widely used, in Quick's original form, as the Probst-Londe modification or as the Quick "intravenous" modification, and many reports of its clinical application and comparison with other tests have been published.<sup>(18)(19)(20)(21)(22)(23)(24)</sup>

#### Methods.

For routine use at Prince Henry Hospital we adopted the technique of Probst<sup>(17)</sup> and Londe—that is, the four-gramme dose, four specimens of urine at intervals of one hour, and the analytical method of Weichselbaum and Probst<sup>(12)</sup>, modified slightly in the following details:

The precipitation is carried out at about 3° C. in a bath of ice and water by the addition of sufficient 10N sulphuric acid to make the urine-salt mixture strongly acid to Congo red paper. After standing in a bath for at least an hour the mixture is filtered by suction through two thicknesses of filter paper (Whatman Number 1, 4.25 centimetres) supported in a Jena sintered glass filter (43GI), and the precipitate is sucked as dry as possible. The flask in which the precipitation has been carried out is then rinsed with a volume of iced 30% sodium chloride solution equal to one-quarter of the volume of the urine-salt mixture, and the rinsings are used to wash the hippuric acid on the filter. The precipitate is again sucked dry. The hippuric acid on the filter, together with the traces remaining in the precipitation flask, is then dissolved in hot water and titrated with N/2 sodium hydroxide solution (phenolphthalein).

Our results are reported in terms of benzoic acid, and for the calculation of the "percentage normal" values we have used the averages of the Probst<sup>(17)</sup> and Londe's<sup>(15)</sup> normal subjects' results, recalculated in terms of benzoic acid instead of sodium benzoate. These averages are approximately as follows: first hour 0.85 grammes, second hour 1.15 grammes, third hour 0.80 grammes, fourth hour 0.20 grammes; total, 3.0 grammes of benzoic acid.

A few tests on apparently healthy subjects gave results closely similar to these averages.

Probst<sup>(17)</sup> and Londe found that the greatest excretion usually occurred in the second hour. In their normal subjects at least five-eighths of the total four-hour excretion occurred in the first two hours, and they suggested shortening the test to the collection of a single specimen two hours after the ingestion of the sodium benzoate. It is true that in most subjects, normal or abnormal, the rate of excretion follows a normal course with a maximum in the second hour; but our results, and those of Henderson and Splatt,<sup>(25)</sup> indicate that the suggested abbreviation would be unsatisfactory. In our series of 170 tests at Prince Henry Hospital, it happened that in 21 the specimens could not be collected at the regular times. Of the remaining 149 tests, 4.5% (3.0%) showed the maximal excretion to be during the first hour, 10% (71.1%) during

the second hour, 37.5% (25.2%) during the third hour, and 1.0 (0.7%) during the fourth hour. If the two-hour test was used, the hepatic function of many of our subjects would be assessed as considerably below normal, merely because the maximal excretion of hippuric acid occurred in the third hour instead of the second. Of the 38 tests which did not show the maximum excretion to be in the first or second hours, 28 produced low two-hour values which were not supported by the three-hour or four-hour values, or by the maximal excretion in any hour.

#### Clinical Results.

In this paper we are considering the results of 226 hippuric acid tests, of which 127 were performed on 90 patients with diseases of the thyroid gland and 43 were performed on 40 other patients at Prince Henry Hospital. The remaining 56 tests were performed on 30 private patients suffering from thyrotoxicosis. (We are indebted to Dr. F. S. Hansman for his collaboration with the last-mentioned tests.)

Quick's work<sup>(11)(12)</sup> has established the hippuric acid test as a test of the conjugating and detoxicating functions of the liver, and as such it has been employed. However, contrary to expectations, the results of the hippuric acid tests in our few fatal cases of thyrotoxicosis did not run parallel with the changes in the hepatic structure. Comparisons of the hippuric acid test with tests for other liver functions<sup>(26)(27)(28)(29)(30)(31)(32)(33)(34)</sup> have shown that these tests tend to vary with each other. Our figures (Tables Ia to VI) show the same tendency, although the correlation is not close.

The numbers allotted to Cases I to LI of this paper correspond to those used previously (Wilson<sup>(35)</sup>) when glucose and galactose tolerance tests were discussed; no relationship was found between the results of these tests and the post-operative reaction. An attempt has been made in this paper to correlate the results of the hippuric acid test and of tests of other liver functions with the post-operative reaction, but also without success. The results of these tests on patients with diseases of the thyroid gland are contained in Tables Ia, Ib, IIa, IIb and III; they are interesting, for they illustrate the possible fallacy of clinical impressions. We had come to believe that there was a definite relationship in thyrotoxicosis between the variations of the response to the hippuric acid test and the post-operative reaction; but an analysis of our figures failed to prove any relationship between the age or sex of the patient, the duration of symptoms, the blood cholesterol, bilirubin and prothrombin levels and the results of the hippuric acid test on the one hand, and the post-operative reaction, as judged by the maximum post-operative pulse rate or temperature or by death of the patient, on the other hand.

This statement needs qualification, for the patients had been prepared for operation as previously described (Poate<sup>(36)</sup>), and only those patients who were considered to have responded satisfactorily were subjected to operation; that is, they were patients for whom we considered the risk of a severe post-operative reaction to be minimal. The operations were performed by two of us (H.R.G.P. and T.E.W.) using the subfascial method.<sup>(37)(38)</sup>

We could satisfy our clinical conscience by assuming that the patients who did not respond to the usual pre-operative preparation would have died if operation had been performed. Yet, even if we suppose that this is true, there would still be no statistical basis for a belief in a definite relationship between the results of the hippuric acid test and the post-operative reaction.

In the cases in which operation was performed and in the fatal cases, the results of the hippuric acid test were found to be independent of the pathological changes in the thyroid glands.

Of the thyrotoxic patients not subjected to operation, four with early Graves's disease preferred medical treatment, and operation on them was deferred. Another patient

<sup>1</sup> In some instances equal excretion in two consecutive hours was obtained. These are scored as "0.5" in each of the two hours.



TABLE IA.  
Cases of Acute Thyrotoxicosis (Prince Henry Hospital).

Case Number.	Patient's Sex and Age. (Years.)	Duration of Symptoms. (Months.)	Basal Metabolic Rate. (Percentage.) <sup>1</sup>	Cholesterol. (Milligrammes per 100 Millilitres of Blood.) <sup>1</sup>	Bilirubin. (Milligrammes per 100 Millilitres of Blood.) <sup>1</sup>	Prothrombin. (Percentage.) <sup>1</sup>	Maximum Pulse Rate After Operation. (Beats per Minute.)	Maximum Temperature After Operation. (Degrees Fahrenheit.)	Remarks and Treatment.	Hippuric Acid Test Result. (Percentage.) <sup>1</sup> <sup>2</sup>
I	F. 55	3	+27 (21/6/41) +14 (12/9/41)	83	0.3	100	120	99.2	Total thyroidectomy. (2/10/41)	101 (23/6/41)] 106 (7/7/41)] 107 (11/9/41)]
IV	M. 23	6	+43	142	0.1	100	100	101.4	Subtotal thyroidectomy.	110
V	F. 19	6	+22	55	0.5	89	130	101.0	Subtotal thyroidectomy (26/8/41).	122 (13/8/41) 113 (20/8/41)
VI	F. 30	6	+76	88	0.3	95	156	104.2	Hemi- thyroidectomy; fatal post- operative thyroid crisis.	100
VII	M. 40	3	+54	—	0.9	94	120	100.4	Subtotal thyroidectomy.	103
VIII	F. 34	13	+66 (4/6/41) -10 (2/7/41)	—	0.1	100	104	99.0	Subtotal thyroidectomy (19/6/41).	101 (5/6/41) 104 (3/7/41)
X	F. 31	3	+54 (26/6/41) -15 (3/7/41) -20 (23/7/41)	128	0.1	100	120	100.4	Subtotal thyroidectomy (10/7/41).	100 (26/6/41) 96 (2/7/41) 100 (26/7/41)
XI	F. 37	4	+56 (17/4/41) +25 (22/5/41) +32 (13/6/41) +35 (18/8/41)	106	0.3	100	140	100.2	Hemi- thyroidectomy (12/5/41). Deep X-ray therapy started (6/6/41).	100 (16/4/41) 93 (30/5/41) 90 (18/6/41) 109 (18/11/41)
XIII	F. 22	60	+50 (23/11/40) +7 (11/5/41)	—	0.2	96	128	99.6	Subtotal thyroidectomy (3/12/40).	103 (3/12/40)] 101 (12/5/41)
XVIII	F. 44	24	+47	—	0.1	70	126	99.2	Subtotal thyroidectomy (24/6/41).	102 (12/6/41) 111 (11/7/41)
XX	M. 52	6	+52	—	0.4	100	—	—	Deep X-ray therapy started (9/8/41).	106 (8/8/41)] 111 (18/9/41)]
XXI	M. 51	4	+62	—	0.3	84	—	—	Deep X-ray therapy started (10/4/41).	92 (9/4/41) 85 (27/5/41)
XXVI	F. 32	4	+63	84	—	100	130	103.2	Death from cardiac failure.	89
XXVIII	F. 36	12	+25	—	—	—	—	—	Hemi- thyroidectomy. Operation deferred.	97
XXIX	F. 42	6	+50	—	—	100	172	101.2	Subtotal thyroidectomy.	104
XXX	F. 26	6	+43	—	—	100	112	99.6	Subtotal thyroidectomy.	99
LIII	F. 35	2	+27	80	0.1	100	120	100.2	Subtotal thyroidectomy.	101
LIV	F. 45	18	+56	68	0.1	96	144	99.4	Right hemi- thyroidectomy.	97
							156	100.2	Left hemi- thyroidectomy.	
LV	F. 34	48	+27	—	—	—	140	100.0	Subtotal thyroidectomy.	101
LVI	F. 36	2	+45	96	0.2	100	—	—	Referred to private doctor.	97
LVII	F. 29	3	+50	—	—	—	120	100.4	Subtotal thyroidectomy.	97
LVIII	F. 38	3	+53	—	—	—	—	—	Treated by deep X-ray therapy.	102
LIX	F. 52	3	+83	116	0.3	96	—	—	Deep X-ray therapy started (13/11/41).	96 (12/11/41) 95 (26/11/41)
LX	F. 25	1	+36	90	0.1	100	128	100.2	Subtotal thyroidectomy.	101
LXI	F. 37	12	+40	—	—	—	—	—	Death from thrombosis of superior longi- tudinal sinus.	101
LXII	F. 47	2	+30	—	—	—	120	100.0	Subtotal thyroidectomy.	78
LXIII	F. 39	12	+15	208	0.1	100	—	—	Operation deferred.	98
LXIV	F. 30	11	+15	93	0.1	100	—	—	Operation deferred.	112
LXV	F. 19	3	+25	90	0.2	100	122	100.8	Subtotal thyroidectomy.	89
LXVI	F. 36	4	+30	130	—	—	130	101.4	Subtotal thyroidectomy (13/11/41).	86 (25/10/41) 95 (11/11/41)
LXVII	F. 26	12	+64	—	—	—	120	99.4	Subtotal thyroidectomy.	87
LXVIII	F. 32	24	+36	76	0.1	100	134	99.6	Subtotal thyroidectomy.	92
LXIX	F. 53	12	+17	—	—	—	112	99.4	Total thyroidectomy (4/12/41).	83 (17/11/41) 91 (30/12/41)
LXX	F. 17	1	+78	143	0.3	—	116	98.4	Hemi- thyroidectomy.	100

<sup>1</sup> The figures for which no dates are given were obtained within a day or two of the patient's admission to hospital.

<sup>2</sup> Expressed as a percentage of the normal excretion (3.0 grammes of benzoic acid excreted in four hours=100%).

TABLE IA.—Continued.  
Cases of Acute Thyrotoxicosis (Prince Henry Hospital).—Continued.

Case Number.	Patient's Sex and Age. (Years.)	Duration of Symptoms. (Months.)	Basal Metabolic Rate. (Percentage). <sup>1</sup>	Cholesterol. (Milligrammes per 100 Millilitres of Blood). <sup>1</sup>	Bilirubin. (Milligrammes per 100 Millilitres of Blood). <sup>1</sup>	Prothrombin. (Percentage). <sup>1</sup>	Maximum Pulse Rate After Operation. (Beats per Minute.)	Maximum Temperature After Operation. (Degrees Fahrenheit.)	Remarks and Treatment.	Hippuric Acid Test Result. (Percentage). <sup>1,2</sup>
LXXI	F. 18	3	+70	—	—	—	124	101.2	Subtotal thyroidectomy.	96
LXXII	F. 37	6	+46	127	0.1	94	110	100.8	Subtotal thyroidectomy.	100
LXXIII	F. 32	6	+66	48	1.0	—	170	102.4	Subtotal thyroidectomy.	102
LXXIV	F. 33	12	+66	66	0.7	98	144	100.8	Subtotal thyroidectomy.	100
LXXV	F. 19	2	+80	50	0.3	98	160	100.0	Subtotal thyroidectomy.	104
LXXVI	F. 49	48	+40	75	0.2	100	130	101.2	Subtotal thyroidectomy.	92
LXXVII	F. 49	12	+36	153	0.1	100	126	100.2	Subtotal thyroidectomy.	86
LXXVIII	F. 36	1	+26	45	0.9	100	120	100.0	Subtotal thyroidectomy.	88
LXXIX	F. 20	6	+48	—	—	100	—	—	Treated by deep X-ray therapy.	98
LXXX	M. 37	5	+37	75	0.1	100	—	—	Treated by deep X-ray therapy.	91
LXXXI	F. 43	4	+19 (22/10/40) —6 (8/2/41)	88	0.1	82	130	100.2	Total thyroidectomy (10/2/41).	102 (22/10/40) 99 (7/2/41)
LXXXII	F. 31	12	+31	106	0.4	100	144	100.8	Subtotal thyroidectomy.	91
LXXXIII	F. 24	1	+83	56	0.3	98	146	100.8	Hemi-thyroidectomy.	88
LXXXIV	F. 50	1	+50	—	—	—	140	100.6	Subtotal thyroidectomy.	103

<sup>1</sup> The figures for which no dates are given were obtained within a day or two of the patient's admission to hospital.

<sup>2</sup> Expressed as a percentage of the normal excretion (3.0 grammes of benzoic acid excreted in four hours=100%).

TABLE IB.  
Acute Thyrotoxicosis. (Private Cases.)

Case Number.	Patient's Sex and Age. (Years.)	Duration of Symptoms. (Months.)	Maximum Pulse Rate After Operation. (Per Minute.)	Maximum Temperature After Operation. (Degrees Fahrenheit.)	Remarks and Treatment. <sup>1</sup>	Hippuric Acid Test. (Percentage). <sup>1,2</sup>
LXXXV	F. 55	6	—	—	Basal metabolic rate +17%. Operation deferred.	72 (30/10/41) 67 (10/11/41)
LXXXVI	F. 54	6	110	100.0	Subtotal thyroidectomy.	95
LXXXVII	F. 48	1	140	100.0	Total thyroidectomy.	82
LXXXVIII	F. 59	12	96	99.8	Total thyroidectomy (14/8/42).	69 (30/7/42) 62 (4/8/42) 74 (11/8/42)
LXXXIX	F. 42	12	100	99.8	Total thyroidectomy.	76
XC	F. 45	15	120	100.4	Subtotal thyroidectomy.	88
XCI	F. 49	8	100	99.5	Total thyroidectomy.	90
XCII	F. 56	12	100	99.8	Total thyroidectomy.	75
XCIII	F. 54	12	140	102.0	Subtotal thyroidectomy.	63
XCIV	F. 46	36	100	99.8	Total thyroidectomy.	74
XCV	M. 57	12	100	99.5	Basal metabolic rate +50%. Total thyroidectomy (25/3/42).	65 (11/3/42) 77 (21/3/42)
XCVI	M. 63	8	140	103.0	Total thyroidectomy.	79
XCVII	F. 48	36	—	—	Treated by deep X-ray therapy.	66

<sup>1</sup> The figures for which no dates are given were obtained within a day or two of the patient's admission to hospital.

<sup>2</sup> Expressed as a percentage of the normal excretion (3.0 grammes of benzoic acid excreted in four hours=100%).

was referred to her private doctor for treatment. The patient in Case LXI died from a thrombosis of the superior longitudinal sinus while being prepared for operation. Seven patients acutely ill with thyrotoxicosis did not respond satisfactorily to the routine pre-operative preparation and were therefore treated by deep X-ray therapy. Two elderly patients suffering from toxic adenomata of the thyroid gland died of cardiac failure soon after their admission to hospital. In three other cases of toxic adenomata of the thyroid, operation was deferred because of severe cardiac failure. Another patient with a toxic adenomatous thyroid also suffered from severe bronchial asthma and chronic bronchitis, and because of the severity of the two last-mentioned lesions it was decided that operation was unwarranted. Similarly, operation was not advised for a patient suffering from both a toxic adenomatous thyroid and advanced chronic nephritis. Three other patients with toxic adenomatous thyroids,

whose pre-operative responses were considered inadequate, were referred for deep X-ray therapy. In the cases of acute thyrotoxicosis and in those of toxic adenomatous thyroid, no relationship was observed between the degree of post-irradiation reaction and the results of the liver function tests.

Details of the nine patients suffering from thyrotoxicosis in this series who died are collected together in Table IV. Death followed thyroid crises in three cases, in two of which the results of the hippuric acid test were 100% and 98% respectively before treatment was begun; in the third case the results of the hippuric acid test improved from 67% to 95% while the patient was being prepared for operation. It would appear, therefore, that impaired conjugating and detoxicating functions of the liver are probably not the only factors in the aetiology of post-operative thyroid crises. In Case XXI the hippuric acid test produced a result of 92% before and 85% after

TABLE II.  
Toxic Adenomatous Thyroid. (Prince Henry Hospital.)

Case Number.	Patient's Sex and Age. (Years.)	Duration of Symptoms. (Months.)	Basal Metabolic Rate. (Percentage). <sup>1</sup>	Cholesterol. (Milligrammes per 100 Millilitres of Blood). <sup>1</sup>	Bilirubin. (Milligrammes per 100 Millilitres of Blood). <sup>1</sup>	Prothrombin. (Percentage). <sup>1</sup>	Maximum Pulse Rate After Operation. (Beats per Minute.)	Maximum Temperature After Operation. (Degrees Fahrenheit.)	Remarks and Treatment.	Hippuric Acid Test Result. (Percentage). <sup>1</sup>
II	F. 49	9	+28 (15/7/41) -5 (5/8/41)	—	0.1	97	120	99.4	Total thyroidectomy (22/7/41).	101 (16/7/41) 92 (4/8/41)
III	F. 70	48	+47	72	0.5	67	—	—	Death from cardiac failure.	27
IX	F. 54	60	+10	—	0.3	96	180	105.0	Total thyroidectomy (10/6/41). Fatal crisis.	67 (21/5/41) 70 (27/5/41) 95 (6/6/41)
XII	M. 63	18	+35	—	1.4	100	—	—	Death from cardiac failure.	81
XIV	F. 59	60	+66	118	0.1	100	120	104.0	Total thyroidectomy (5/8/41).	89 (18/7/41) 89 (30/7/41)
XV	F. 47	48	+14 (5/8/41) -28 (21/8/41)	125	0.1	94	116	99.6	Total thyroidectomy (14/8/41).	102 (6/8/41) 95 (23/8/41) 105 (30/8/41)
XVI	M. 60	12	+35 (16/7/41) +22 (30/7/41)	70	0.7	—	—	—	Severe cardiac failure. Opera- tion deferred.	77 (10/7/41) 80 (21/7/41) 102 (5/8/41)
XXIII	M. 49	24	+24	42	0.3	100	148	100.0	Subtotal thyroidectomy.	88
XCVIII	M. 63	5	+59	—	0.1	98	92	98.4	Total thyroidectomy (6/3/41).	65 (17/2/41) 94 (3/3/41)
XCIX	F. 50	12	+34	—	—	—	—	—	Bronchial asthma. Operation de- ferred.	78 (16/12/41) 91 (5/1/42)
C	F. 60	9	+75	98	0.2	94	—	—	Treated by deep X-ray therapy.	64 (11/11/41) 86 (5/2/42)
CI	F. 34	24	+13	88	0.1	100	120	100.0	Subtotal thyroidectomy.	102
CH	F. 56	4	+24	—	—	90	110	99.4	Total thyroidectomy.	73
CHH	F. 60	12	+30	104	0.2	100	120	99.4	Total thyroidectomy (10/12/41).	112 (2/12/41) 95 (29/12/41)
CIV	F. 49	60	+39	—	—	—	140	102	Subtotal thyroidectomy.	91
CV	M. 70	6	+32	58	0.9	100	—	—	Treated by deep X-ray therapy.	53
CVI	M. 55	2	+40	63	0.4	100	170	102.2	Hemi- thyroidectomy (18/12/41).	98 (20/11/41) 87 (11/12/41)
CVII	M. 48	6	+43	—	—	—	130	103.0	Total thyroidectomy.	103 (7/1/42) 100
CVIII	F. 49	6	+41	85	0.2	96	140	99.2	Total thyroidectomy.	93
CIX	F. 35	3	+19	—	—	92	—	—	Associated chronic nephritis. Operation de- ferred.	79
CX	F. 58	12	+50	174	0.1	85	120	99.2	Total thyroidectomy.	101
CXI	F. 59	36	+45	50	0.4	100	108	98.9	Total thyroidectomy. Death from cardiac failure.	61 (29/11/41) 62 (18/12/41) 74 (29/12/41)
CXII	F. 58	96	+20	210	0.1	100	180	104.6	Total thyroidectomy. Fatal crisis.	98

<sup>1</sup> The figures for which no dates are given were obtained within a day or two of the patient's admission to hospital.

<sup>2</sup> Expressed as a percentage of the normal excretion (3.0 grammes of benzoic acid excreted in four hours=100%).

a course of deep X-ray therapy, necessitated by the patient's failure to respond to the usual pre-operative preparation. Clinically, this patient was considered too bad a "risk" for operation, though this was not indicated by the hippuric acid test. Death occurred from cardiac failure soon after the completion of the course of deep X-ray therapy. In Cases CXI and CXIX death occurred from cardiac failure within six weeks of operation. In Case CXIX the hippuric acid test produced a result of 84% before treatment was begun; and in Case CXI the results of the hippuric acid test improved from 61% to 74% whilst the patient was being prepared for operation.

#### Diseases of the Liver and Other Organs.

Tables V and VI contain the results of the hippuric acid and other tests in cases of diseases of the liver and gall-bladder and in a mixed group of cases. Impairment of liver function in those patients suffering from organic diseases of the liver was to be expected and needs no comment. In Tables V and VI there is again no direct relationship between the results of the hippuric acid test

and the post-operative reaction. In Case CLXV (essential hypertension), the low result elicited by the hippuric acid test (28%) was probably related to the impairment of renal function. The level of the patient's blood urea was 87 milligrammes per 100 millilitres, and the urea concentration test produced a result of 1.1%, 0.9%, 1.0% and 1.1%, the volume of urine passed in each specimen being less than 50 millilitres.

#### Discussion.

Thyroid crises are notoriously difficult to treat successfully. Because of this, interest has been stimulated and attempts have been made to prevent their development and to determine in which patients they may be expected to develop. The resemblance between thyroid crises and the so-called "liver deaths" of patients suffering from diseases of the liver or gall-bladder was first commented on by Heyd in 1931. Since then this theory has been championed by Lahey.<sup>(20)</sup> By ligation of a branch of the hepatic artery Sutton<sup>(21)(22)</sup> produced a similar syndrome in dogs. The well-recognized, albeit rare, association of jaundice and



TABLE III.  
Toxic Adenomatous Thyroid. (Private Cases.)

Case Number.	Patient's Sex and Age. (Years.)	Duration of Symptoms. (Months.)	Maximum Pulse Rate After Operation. (Per Minute.)	Maximum Temperature After Operation. (Degrees Fahrenheit.)	Remarks and Treatment. <sup>1</sup>	Hippuric Acid Test. (Percentage). <sup>2</sup>
CXIII	F. 60	6	115	100.0	Total thyroidectomy (fibrillation).	71
CXIV	F. 53	2	100	100.0	Total thyroidectomy (22/9/41).	45 (22/8/41)
						52 (1/9/41)
						92 (8/9/41)
						100 (17/9/41)
CXV	F. 60	60	110	100.6	Total thyroidectomy (11/8/42).	46 (14/7/42)
						69 (28/7/42)
						96 (7/8/42)
CXVI	F. 58	24	90	99.0	Total thyroidectomy (28/11/41)	44 (6/11/41)
						103 (17/11/41)
						89 (22/11/41)
CXVII	F. 54	24	100	99.0	Hemithyroidectomy (fibrillation).	73
CXVIII	F. 62	480	—	—	Operation deferred. Advanced cardiac failure.	58
CXIX	F. 73	240	130	100.0	Total thyroidectomy. Fatal cardiac failure.	84
CXX	F. 72	24	—	—	Operation not advised. Advanced cardiac failure.	46 (12/7/42)
						69 (19/7/42)
						96 (26/7/42)
						52 (9/7/42)
CXXI	F. 58	72	130	100.2	Total thyroidectomy (31/7/42).	77 (17/7/42)
						93 (27/7/42)
CXXII	F. 62	60	105	99.8	Total thyroidectomy.	79
CXXIII	F. 55	48	100	99.0	Total thyroidectomy.	98
CXXIV	F. 51	24	120	99.5	Hemithyroidectomy.	88
CXXV	F. 53	96	160	103.0	Total thyroidectomy (23/3/42).	41 (10/2/42)
						63 (23/2/42)
						72 (6/3/42)
						77 (17/3/42)
CXXVI	F. 50	36	120	101.0	Total thyroidectomy (10/10/42).	53 (15/9/42)
						115 (22/9/42)
						59 (29/9/42)
						78 (6/10/42)
CXXVII	F. 49	300	120	100.0	Total thyroidectomy (fibrillation).	81
CXXVIII	M. 63	9	100	99.8	Total thyroidectomy (2/6/42).	55 (25/4/42)
						80 (11/5/42)
						88 (29/5/42)
CXXIX	M. 67	72	—	—	Treated by deep X-ray therapy. Basal metabolic rate +22%.	52 (21/10/41)
						59 (28/10/41)
						53 (8/11/41)
						53 (17/11/41)

<sup>1</sup> The figures for which no dates are given were obtained on the day after the patient's admission to hospital.

<sup>2</sup> Expressed as a percentage of the normal excretion (3.0 grammes of benzoic acid excreted in four hours = 100%).

thyreotoxicosis attracted attention to the liver, which has provided a fruitful source of study, both in man<sup>(42) (43) (44) (45) (46) (47)</sup> and in laboratory animals.<sup>(48) (49) (50)</sup> Rarely, acute yellow atrophy has been described as a complication of thyreotoxicosis.<sup>(47) (51)</sup> To the changes in the liver have been attributed the infrequent jaundice and the more common interference with the response to liver function tests; but it must be remembered that in addition to the specific effect of thyreotoxicosis on the liver, jaundice in thyreotoxic patients may result from cardiac failure or from some unrelated disease, such as catarrhal jaundice or cholelithiasis.

Originally the results of liver function tests were adduced in favour of the belief that thyroid crises were examples of "liver deaths". More recently, however, Haines, Magath and Power<sup>(52)</sup> reported patients with thyroid crises who did not exhibit the expected degree of impaired excretion of hippuric acid, and some doubt has been cast on Lahey's theory. The lack of correlation in our cases of thyreotoxicosis between the results of the hippuric acid and other tests and the post-operative reaction is also in accord with the suggestion that acute liver failure is not the sole cause of thyroid crises.

It is not our intention to question the fact that an estimate may be obtained of the conjugating and detoxicating functions of the liver by the hippuric acid test, or that these functions may be impaired in thyreotoxicosis;<sup>(53) (54) (55) (56) (57) (58) (59) (60)</sup> but it is interesting to note that in our cases this impairment was greatest in patients with toxic adenomatous thyroids. This is shown in Tables Ia, Ib, IIa and IIb, and graphically in Figures I and II. The results of the tests on patients with non-toxic adenomatous thyroids are shown in Table III and Figure III.

Excepting occasionally, when a patient had to be omitted owing to the stress of routine work, the series of thyreotoxic patients investigated at Prince Henry Hospital (Tables Ia and IIa) consisted of those consecutively

admitted to hospital, and so far as any hospital population may, they comprise a representative group of patients suffering from thyreotoxicosis. Similarly, our patients with non-toxic adenomatous thyroids (Table III) may be regarded as a representative group of such patients. In the private cases, however, the tests were performed only

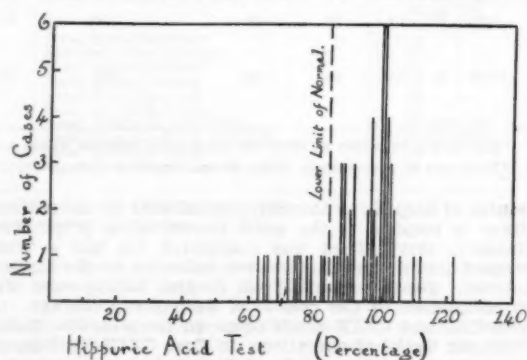


FIGURE I.

To show the distribution of the results of the hippuric acid test in 61 cases of acute thyreotoxicosis. These results were obtained within a day or two of the admission of the patients to hospital.

on those patients suffering from thyreotoxicosis with regard to whom it was anticipated that the knowledge to be derived from the tests would be advantageous in estimating the efficacy of and response to pre-operative treatment; that is, they consisted of a selected group of patients, who on clinical grounds were regarded as "poor operative risks".

TABLE III.  
Non-toxic Adenomatous Thyreoid.

Case Number.	Patient's Sex and Age. (Years.)	Duration of Symptoms. (Months.) <sup>1</sup>	Basal Metabolic Rate. Percentage. <sup>2</sup>	Cholesterol. (Milligrammes per 100 Millilitres of Blood.) <sup>3</sup>	Bilirubin. (Milligrammes per 100 Millilitres of Blood.) <sup>3</sup>	Pro-thrombin. (Percentage.) <sup>3</sup>	Maximum Pulse Rate After Operation. (Per Minute.)	Maximum Temperature After Operation. (Degrees Fahrenheit.)	Remarks and Treatment.	Hippuric Acid Test. (Percentage.) <sup>2, 3</sup>
XXXI	F. 36	6	+26	—	—	88	—	—	Associated chronic myeloid leucemia.	85
XXXIII	F. 20	12	-3	—	0.5	100	120	100.0	Subtotal thyroidectomy.	104
XXXVIII	F. 55	1	-1	—	0.3	100	130	99.6	Subtotal thyroidectomy.	96
XXXIX	F. 25	9	+15	30 (15/5/41) 393 (24/5/41) 165 (26/5/41)	0.4	100	130	99.0	Subtotal thyroidectomy (12/6/41). Associated diabetes mellitus.	87
XL	F. 30	36	-15	225	0.2	98	104	98.4	Hemi-thyroidectomy (17/7/41).	104 (14/7/41) 100 (1/8/41)
XLI	F. 28	12	+8	63	0.1	100	120	99.6	Subtotal thyroidectomy.	95
XLII	F. 38	4	+6	145	0.1	100	—	—	Operation deferred.	100
XLIV	F. 39	6	+4	90	0.5	94	120	99.0	Subtotal thyroidectomy (28/8/41).	72 (12/8/41) 102 (27/8/41) 102 (10/9/41)
LI	M. 28	6	+3	80	0.1	100	136	102.0	Subtotal thyroidectomy.	100
CXXX	F. 63	12	+13	—	—	—	112	99.8	Total thyroidectomy.	89
CXXXI	F. 48	24	+3	—	0.3	100	180	103.0	Hemi-thyroidectomy. Post-operative broncho-pneumonia.	98
CXXXII	F. 50	72	-4	—	0.4	100	108	100.2	Total thyroidectomy. Operation deferred.	100
CXXXIII	F. 49	2	-7	263	0.1	91	—	—	Total thyroidectomy.	105
CXXXIV	F. 56	72	-4	200	0.1	100	140	102.0	Post-operative broncho-pneumonia.	97
CXXXV	F. 32	12	+2	175	0.2	100	108	99.0	Subtotal thyroidectomy.	94
CXXXVI	F. 24	18	-5	67	0.1	100	—	—	Operation deferred.	105
CXXXVII	F. 33	2	+4	124	0.1	100	144	100.2	Hemi-thyroidectomy.	99
CXXXVIII	F. 49	30	-5	—	0.1	100	100	98.6	Hemi-thyroidectomy.	103
CXXXIX	F. 41	18	-5	—	—	—	106	99.6	Subtotal thyroidectomy.	98

<sup>1</sup> The length of time since the enlargement of the thyreoid was first noticed.<sup>2</sup> The figures for which no dates are given were obtained within a day or two of the patient's admission to hospital.<sup>3</sup> Expressed as a percentage of the normal excretion (3.0 grammes of benzoic acid excreted in four hours=100%).

If we exclude the male patients, of whom there were only a few, and analyse the results of the hippuric acid tests on the female patients of Tables Ia, IIa and III, we

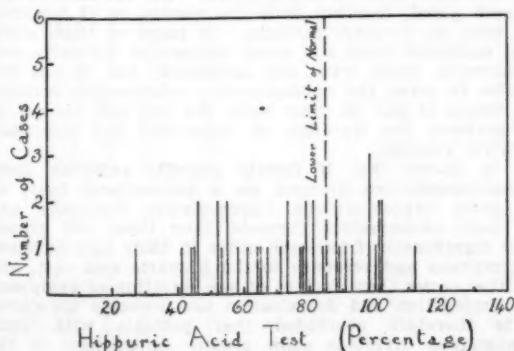


FIGURE II.

To show the distribution of the results of the hippuric acid test in 40 cases of toxic adenomatous thyreoid. These results were obtained within a day or two of the admission of the patients to hospital.

find that the results of the hippuric acid tests of Table IIa (toxic adenomatous thyreoid) are significantly different from those of Table Ia (acute thyreotoxicosis) and from

those of Table III (non-toxic adenomatous thyreoid), but that there is no significant difference between the results in the latter two groups. (The difference of the means of

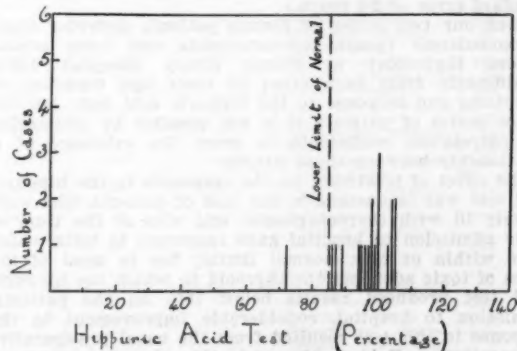


FIGURE III.

To show the distribution of the results of the hippuric acid test in 19 cases of non-toxic adenomatous thyreoid. These results were obtained within a day or two of the admission of the patients to hospital.

the results of the hippuric acid tests in Tables Ia and IIa was 13.8% with a standard error of this difference of 5.8%; for Tables IIa and III the difference was 12.6% with

TABLE IV.  
Fatal Cases of Thyreotoxicosis. (Prince Henry Hospital, 1941.)

Case Number.	Patient's Sex and Age. (Years.)	Duration of Symptoms. (Months.)	Basal Metabolic Rate. (Percentage.) <sup>1</sup>	Cholesterol. (Milligrammes per 100 Millilitres of Blood.) <sup>1</sup>	Bilirubin. (Milligrammes per 100 Millilitres of Blood.) <sup>1</sup>	Prothrombin. (Percentage.) <sup>1</sup>	Maximum Pulse Rate After Operation. (Per Minute.)	Maximum Temperature After Operation. (Degrees Fahrenheit.)	Diagnosis, Treatment, Remarks.	Hippuric Acid Test. (Percentage.) <sup>1</sup>
VI	F. 30	6	+76	88	0.3	95	158	104.2	Acute thyreotoxicosis. Hemithyroidectomy. Post-operative thyroid crisis.	100
XXI	M. 51	4	+62	—	0.3	84	—	—	Acute thyreotoxicosis. Started deep X-ray therapy 11/4/41. Death from cardiac failure.	92 (9/4/41) 85 (27/5/41)
LXI	F. 37	12	+40	—	—	—	—	—	Acute thyreotoxicosis. Death from thrombosis of the superior longitudinal sinus.	101
III	F. 70	48	+47	72	0.5	67	—	—	Toxic adenomatous thyroid. Death from cardiac failure. Operation not performed.	27
IX	F. 54	60	+19	—	0.3	96	180	105.0	Toxic adenomatous thyroid. Total thyroidectomy (10/6/41). Fatal thyroid crisis.	67 (21/5/41) 70 (27/5/41) 95 (6/6/41)
XII	M. 63	18	+35	—	1.4	100	—	—	Toxic adenomatous thyroid. Operation not performed. Death from cardiac failure.	81
CXI	F. 50	36	+45	50	0.4	100	108	98.8	Toxic adenomatous thyroid. Total thyroidectomy. Death from cardiac failure.	61 (29/11/41) 62 (18/12/41) 74 (28/12/41)
CXII	F. 58	96	+20	210	0.1	100	180	104.6	Toxic adenomatous thyroid. Fatal thyroid crisis.	98
CXIX	F. 73	240	—	—	—	—	130	100.0	Toxic adenomatous thyroid. Total thyroidectomy. Fatal cardiac failure.	84

<sup>1</sup> The figures for which no dates are given were obtained within a day or two of the patient's admission to hospital.

<sup>2</sup> Expressed as a percentage of the normal excretion (3.0 grammes of benzoic acid excreted in four hours = 100%).

a standard error of 6.1%; and for tables Ia and III the difference was 1.2% with a standard error of 2.4%.

If the male patients are again excluded, a comparison of the figures in Table Ia with those of Table IIa reveals that there are significant differences between the ages of the patients and also between the durations of toxic symptoms, but not between the blood cholesterol, bilirubin or prothrombin levels in these two groups. (In Tables Ia and IIa the difference between the means of the durations of symptoms is 22.8 months, with a standard error of 7.5 months, and the difference between the means of the ages of the patients in these two groups is 18.5 years, with a standard error of 2.8 years.)

Thus our two series of female patients suffering from thyreotoxicosis (acute thyreotoxicosis and toxic adenomatous thyroids) at Prince Henry Hospital differ significantly from each other in their age, duration of symptoms and response to the hippuric acid test; but for either series of patients it is not possible by estimating the correlation coefficients to prove the existence of a relationship between these figures.

The effect of treatment on the responses to the hippuric acid test was inconstant in the case of patients who were acutely ill with thyreotoxicosis, and who at the time of their admission to hospital gave responses to tests which were within or near normal limits; but in most of the cases of toxic adenomatous thyroid in which the hippuric acid test produced results below 70% on the patients' admission to hospital, considerable improvement in the response to this test resulted from the usual pre-operative preparation. Tables IIa and IIb show an average increase per week of 7.1% in the results of the hippuric acid test. This may be regarded as confirmatory evidence of the value of the pre-operative treatment employed.

#### Summary and Conclusions.

The best measure of hepatic function given by the hippuric acid test is probably the maximal rate of con-

jugation, which for practical purposes may be estimated by the greatest hourly excretion of hippuric acid. For clinical purposes, however, we have used the "percentage normal" calculated on the total four hours' excretion; but unless the three-hour, the four-hour and maximal hourly excretions are in substantial agreement, we consider that the result is unreliable. The four-hour fractional test is preferred; but where circumstances necessitate a shortening of time and labour, the three-hour single specimen test appears to be the method of choice.

In this paper we have discussed the results of 183 hippuric acid tests on 133 patients with diseases of the thyroid gland, together with the results of 43 hippuric acid tests on 40 other patients. In many of these cases basal metabolic rates and blood cholesterol, bilirubin and prothrombin levels were also estimated; but it was not possible to prove the existence of a relationship between the results of any of these tests, the age and the sex of the patients, the duration of symptoms and the post-operative reaction.

It is shown that if female patients suffering from thyreotoxicosis are grouped on a pathological basis as (i) acute thyreotoxicosis (hyperplastic thyroid) and (ii) toxic adenomatous thyroid, then these two groups differ significantly from each other in their age, duration of symptoms and response to the hippuric acid test, and in either series these factors of age, duration of symptoms and conjugation and detoxication are probably unrelated. It is therefore concluded that patients with toxic adenomatous thyroids show greater impairment of the conjugating and detoxicating function of the liver than do patients with acute thyreotoxicosis, and that this difference is not entirely due to the longer duration of symptoms or to the increased age of the former group of patients.

In the nine fatal cases of thyreotoxicosis of this series, the results of the hippuric acid test were not proportional to the changes in hepatic structure; nor was there any relationship between the results of the hippuric acid test



TABLE V.  
Diseases of the Liver and Gall-Bladder.

Case Number.	Patient's Sex and Age. (Years.)	Duration of Symptoms. (Months.)	Cholesterol. (Milligrammes per 100 Millilitres of Blood.) <sup>1</sup>	Bilirubin. (Milligrammes per 100 Millilitres of Blood.) <sup>1</sup>	Prothrombin. (Percentage.) <sup>1</sup>	Maximum Pulse Rate After Operation. (Per Minute.)	Maximum Temperature After Operation. (Degrees Fahrenheit.)	Diagnosis and Remarks.	Hippuric Acid Test. (Percentage.) <sup>2</sup>
XXXIV	M. 42	2	—	5.5	75	110	100.6	Carcinoma of the common bile duct. Death four weeks after operation. Cachexia.	48
XXXVI	M. 40	12	—	2.3	—	—	—	Hemochromatosis.	95
XLV	M. 70	24	88	0.3	73	120	98.8	Chronic cholecystitis and subacute hepatitis. Cholecystectomy.	93
XLVII	F. 62	4	—	0.5	95	110	99.0	Cirrhosis of the liver. Laparotomy (24/7/41).	103 (21/7/41)
XLVIII	F. 56	56	580	5.9	75	—	—	Metastatic carcinoma of the liver.	37 (7/8/41)
CXL	M. 20	1	—	5.6	—	130	100.6	Diaphragmatic hernia. Hepatomegaly. Laparotomy. Death two days after operation. This case has been reported elsewhere. <sup>30</sup>	50
CXLI	F. 60	2	—	0.4	—	108	100.2	Cholelithiasis. Cholecystectomy.	93
CXLII	M. 46	48	—	—	86	104	99.4	Cholelithiasis. Cholecystectomy.	83
CXLIII	M. 42	6	180	0.4	90	110	99.2	Cholelithiasis. Cholecystectomy.	105
CXLIV	F. 60	1	—	0.5	94	108	99.0	Cholelithiasis. Cholecystectomy.	120
CXLV	F. 60	60	—	—	—	104	99.6	Chronic cholecystitis. Cholecystectomy.	107
CXLVI	M. 50	72	—	0.5	—	96	99.0	Chronic cholecystitis. Cholecystectomy.	100
CXLVII	M. 54	36	68	1.7	73	—	—	Cirrhosis of the liver. Fatal haematemesis.	76
CXLVIII	M. 11	1	—	—	—	—	—	Congenital syphilis. Hepatomegaly.	78 (11/9/41)
CXLIX	M. 56	9	—	0.3	94	124	100.0	Carcinoma of the rectum. Hepatic metastases. Laparotomy.	106 (22/9/41)
CL	M. 50	3	—	5.4	73	114	99.0	Carcinoma of the pancreas. Hepatic metastases. Laparotomy. Death 18 days later.	84

<sup>1</sup> The figures for which no dates are given were obtained within a day or two of the patient's admission to hospital.<sup>2</sup> Expressed as a percentage of the normal excretion (3.0 grammes of benzoic acid excreted in four hours × 100%).TABLE VI.  
Miscellaneous Conditions.

Case Number.	Patient's Sex and Age. (Years.)	Duration of Symptoms. (Months.)	Basal Metabolic Rate. (Percentage.) <sup>1</sup>	Cholesterol. (Milligrammes per 100 Millilitres of Blood.) <sup>1</sup>	Bilirubin. (Milligrammes per 100 Millilitres of Blood.) <sup>1</sup>	Prothrombin. (Percentage.) <sup>1</sup>	Maximum Pulse Rate After Operation. (Per Minute.)	Maximum Temperature After Operation. (Degrees Fahrenheit.)	Diagnosis, Treatment, Remarks.	Hippuric Acid Test. (Percentage.) <sup>2</sup>
XXXV	F. 32	60	—	—	—	—	—	—	Chronic pulmonary tuberculosis.	105
XXXVII	F. 07	6	-26	390	0.3	100	—	—	Myxedema treated with thyroxin.	87 (10/5/41)
XLVI	F. 27	6	-15	—	—	—	—	—	Anxiety neurosis.	90 (20/6/41)
CLI	F. 63	3	+1	—	1.3	100	—	—	Pernicious anaemia.	97
CLII	M. 52	48	—	162	—	—	—	—	Chronic gout.	98
CLIII	F. 43	12	+3	—	0.8	88	—	—	Anxiety neurosis.	110
CLIV	F. 59	6	+4	155	0.3	91	—	—	Anxiety neurosis.	96
CLV	F. 21	9	+14	35	—	98	—	—	Anxiety neurosis.	106
CLVI	F. 43	48	-1	245	0.3	94	—	—	Anxiety neurosis.	101
CLVII	F. 29	84	+9	108	0.1	100	—	—	Anxiety neurosis.	105
CLVIII	F. 42	60	+26	80	0.1	97	—	—	Disseminated sclerosis.	85
CLIX	M. 19	12	—	—	—	—	—	—	Spondylitis.	108
CLX	F. 41	48	+9	235	0.1	100	120	99.2	Fibromyoma uteri; hysterectomy.	95
CLXI	F. 36	9	+11	164	0.1	85	110	99.0	Chronic tonsillitis; tonsillectomy.	113
CLXII	F. 30	72	+8	75	0.1	100	94	98.4	Endometritis; curettage of the uterus.	106
CLXIII	F. 52	4	-12	—	—	—	—	—	Post-operative myxoedema.	104
CLXIV	M. 59	36	+5	190	0.6	100	—	—	Arteriosclerosis.	112
CLXV	F. 42	6	+6	—	—	—	—	—	Essential hypertension.	28
CLXVI	M. 54	15	+3	320	0.1	96	—	—	Arteriosclerosis.	123
CLXVII	F. 41	48	+1	103	0.4	—	—	—	Coronary sclerosis.	101
CLXVIII	M. 46	1	+8	—	—	—	—	—	Hypertensive cardiac failure. Death after two weeks in hospital.	113
CLXIX	F. 45	24	+2	—	0.3	96	—	—	Hypertensive cardiac failure.	105
CLXX	F. 56	3	+6	—	—	—	—	—	Essential hypertension.	85
CLXXI	M. 48	36	-4	—	—	—	—	—	Arteriosclerosis.	102
CLXXII	F. 28	2	0	—	—	—	—	—	Paroxysmal tachycardia.	67

<sup>1</sup> The figures for which no dates are given were obtained within a day or two of the patient's admission to hospital.<sup>2</sup> Expressed as a percentage of the normal excretion (3.0 grammes of benzoic acid excreted in four hours = 100%).<sup>3</sup> Blood urea, 67 milligrammes per centum. Urea concentration test: 1.1%, 0.9%, 1.0%, 1.1%; volume each hour, less than 50 millilitres.

and the pathological changes in the thyroid gland in those cases in which this gland was removed at operation or autopsy.

It is concluded that impaired liver function is not the sole cause of thyroidal crises, and that from pre-operative hippuric acid tests it is not possible to determine in which cases these crises will develop.

We do not wish to convey the impression that the hippuric acid or any other test has usurped clinical judgement in the treatment of thyrotoxicosis; rather, these tests are subservient to it. The chief uses of the hippuric acid test in thyrotoxicosis would appear to be in confirming the beneficial effect of pre-operative treatment and in helping to establish the unsuitability of some patients for operation, especially many of those elderly patients with toxic adenomatous thyroids in whom the toxic state has existed for several years.

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## Reports of Cases.

### BLACKWATER FEVER: REVIEW OF A CASE.

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DURING this war the army in Papua has found that the strongest enemy to be faced is malaria. Blackwater fever has long been known in association with malignant tertian malaria. It is capable of becoming a menace to malarious troops who have had inadequate treatment. It seems worth while, therefore, to describe the following severe case of blackwater fever, which appears to have been the first to occur in an Australian military hospital in this area.

#### Clinical Record.

The patient, an Australian sergeant, aged twenty-eight years, was admitted to a casualty clearing station on the evening of November 8, 1942. He stated that in March, 1942, he had been sent to an isolated coastal supply depot where there was no medical officer. He was taking the recommended suppressive dose of five grains of quinine per day as an anti-malarial precaution; but in May, 1942, he suffered from fever accompanied by repeated attacks of shivering. Assuming this to be malaria, he gave himself thirty grains of quinine each day for three days, and remained in bed until he felt better. The fever recurred in a few weeks, but after several days of self-administered quinine he again felt well. He continued to take quinine every day, but increased the dose to ten grains.

On about five other occasions during the following months he felt ill with fever and shivering, but he was able to carry on his duties and was not greatly concerned about his health. Early in November he was transferred to the Moresby area, where he was able to rest for a few days. Two days before his admission to hospital he again felt feverish and shivering; accordingly, as was his custom, he took a large dose of quinine and remained in bed, this time without relief. The fever continued, and on the next day he had further shivering, developed severe abdominal pain, and began to pass large volumes of dark red urine. On the morning of his admission to hospital he had another severe attack of shivering; the abdominal pain became worse and he felt weak and exhausted. Headache became intense, and he again passed a large volume of deeply coloured urine.

During examination he was quiet and listless. He was obviously very ill—emaciated and pallid, but not jaundiced. His temperature was 104° F. The skin was hot, and he was sweating freely. The pulse rate was 100 per minute. The liver was found to be enlarged and tender, and the spleen was palpable four fingers' breadth below the costal margin. He was exquisitely tender in both loins and in the lower part of the abdomen. The urine was opaque and dark red, and obviously contained large amounts of altered blood. No spectroscope was available, but biochemical tests were applied and confirmed the presence of both blood and bile pigments. The reaction of the urine was found to be strongly acid. Blood examination revealed that the red cells numbered 2,500,000 per cubic millimetre, although the hæmoglobin value appeared to be high (11 grammes *per centum*). As a preliminary to blood transfusion, a sample of the patient's serum was obtained and noted to be deeply bile-stained—a fact which explained the unexpectedly high hæmoglobin value. Smears of the patient's blood were made; in the thick film one or two small rings of *Plasmodium falciparum* were seen, but in the thin film no parasites could be detected. The diagnosis of blackwater fever was made.

It was decided that the general condition of the patient did not call for immediate blood transfusion, so he was given a dose of "Luminal" to relieve his apprehension and induced to take fluids by mouth. In spite of retching he was able to drink very freely. A solution of 40 grains of potassium citrate and 20 grains of sodium bicarbonate was given at intervals of two hours, and after a few doses the reaction of the urine became alkaline. A dose of 0.1 gramme of "Atebrin" was given that night.

On the following morning the patient felt and looked worse. His conjunctivæ had a faint icteric tinge. During the morning a dramatic change occurred in his condition. Jaundice rapidly appeared, and by midday his skin was bright yellow. By 11 a.m. his pulse rate had increased to

130 per minute; he was restless, with deep hurried respiration; he was complaining bitterly of abdominal pain and utter weakness. His pallor had become extreme, and enhanced by the yellow colour of the skin, provided a striking appearance. He continued to drink well and to pass large volumes of urine, but the pigmentation of the urine was more intense. Blood transfusion seemed imperative. He was rapidly given 1,200 cubic centimetres of blood, and a slow continuous intravenous infusion of a 5% solution of glucose in normal saline solution was commenced. During the evening he had a mild rigor, but his condition seemed slightly improved and the abdominal pain was much less. The administration of 0.1 gramme of "Atebrin" was continued three times a day.

On the third day he felt no better, and the urine was darker and redder. Despite the blood transfusion, the number of red cells had fallen to 2,000,000 per cubic millimetre, so a further blood transfusion of 700 cubic centimetres was given. He immediately had a mild rigor and the temperature rose to 105° F. That evening the temperature had fallen to 98° F., and the patient seemed more comfortable. The enlargement of liver and spleen was very much less. He still drank freely and continued to pass large volumes of dark urine.

On the fourth day he felt well; the temperature was normal and the jaundice was less. Recovery appeared to have commenced, but the number of red cells had not risen. He spent a comfortable day and his appetite returned. The urine became lighter in colour and by evening was a pale brownish yellow.

On the morning of the fifth day the patient still felt well and the number of red cells had reached 2,750,000 per cubic millimetre; but during the morning his condition suddenly and rapidly deteriorated, and it appeared that the illness had recurred. He complained of headache, vomited several times and had a mild rigor, and his temperature rose to 100° F. The abdominal pain returned, and he was now unable to take fluids. On examination, the liver and spleen were found to be tender and easily palpable. The urine was again dark, but the jaundice continued to fade. Examination of a thick blood smear revealed no malarial parasites, but in a thin smear a number of immature red cells and a few erythroblasts were seen. A transfusion of 600 cubic centimetres of blood was given, but the urine became even darker and his general condition was worse.

On the morning of the sixth day he was extremely exhausted and still complained of abdominal pain. His temperature remained high, and it was decided to increase the daily dose of "Atebrin" to 0.6 gramme. The urine was nearly black in colour, and the number of red cells having fallen to 1,800,000 per cubic millimetre, a blood transfusion of 700 cubic centimetres was given. That afternoon the number of red cells had fallen still further to 1,500,000 per cubic millimetre. That evening the patient appeared gravely ill and was having a continued mild rigor.

On the morning of the seventh day the patient felt and looked much better, and his temperature had fallen. His abdominal pain was less and the enlargement of spleen and liver was diminished. But the urine was brownish black, and it was stained more darkly than previously. The red cells stained poorly and showed anisocytosis and polikilocytosis; erythroblasts, myelocytes and numerous metamyelocytes were present, so it was decided to give four cubic centimetres of "Anahæmin" liver extract by intramuscular injection. As the red cells still numbered only 2,100,000 per cubic millimetre, another blood transfusion of 700 cubic centimetres was given.

On the eighth day the patient felt better and appeared to have overcome his illness. The spleen was just palpable and not tender. The urine was dark brown in colour. The red cells numbered only 2,500,000 per cubic millimetre of blood, so another transfusion of 1,600 cubic centimetres was given.

The next morning he was brighter and stronger. The administration of "Atebrin" was discontinued, and a mixture of ferrous sulphate was given. Another injection of "Anahæmin" was given, and he was put on a full diet.

By the twelfth day the patient was well and active. The spleen was not palpable, the urine was a normal colour and the number of red cells had risen to 3,700,000 per cubic millimetre. No course of "Plasmoquine" was given, in view of the possibility of its poisonous effects such as severe abdominal pain. It was thought not justifiable that the patient should remain exposed to the danger of reinfection in Papua, so it was recommended that he be evacuated to Australia as quickly as possible, to continue his convalescence and to complete anti-malarial treatment. He was warned of the grave danger to himself of another attack of blackwater fever and was advised not to return to the



tropics. A few days later he left by hospital ship. In a personal note he later reported that he was quite well, but gave no clinical details.

#### Commentary.

This case was a very severe one, and was characterized by most of the usually described features of blackwater fever. It presumably occurred six months after infection with malignant tertian malaria; this is a rather short interval, although Manson-Bahr<sup>(1)</sup> refers to a case which occurred eight days after the original infection.

The most prominent feature of the illness is the occurrence of acute hemolytic crises accompanied by sharp rises in temperature and severe rigors. These pyrexial attacks are depicted in Figure I; the temperature is seen to return to normal as each hemolytic crisis subsides. The severity of this blood destruction is also demonstrated in Figure I, in which the daily variation in the number of red cells is shown graphically. The red cell count was the indication

large blood transfusion. On the eighth day the crisis was obviously overcome, and the rise in the number of red cells now roughly corresponded to the volume of blood transfused.

The sudden appearance of jaundice and its rapid intensification are also features of this disease; when this phenomenon is seen it indicates that the illness is serious—that hemolysis is very active. The sudden onset in this case is illustrated in Figure I. It is of great interest to note that during the second series of hemolytic crises the jaundice did not appreciably deepen; moreover, the urine was brown and not red as during the primary crises.

In blackwater fever there is often sudden anuria, which may bring about a fatal termination; but fortunately this patient was still passing large quantities of urine when he was admitted to hospital.

#### Discussion.

The aetiology of blackwater fever is still indefinite. It is usual to find a history of irregular administration of quinine; but blackwater fever may occur in patients who have never taken quinine or who have taken "Atebrin" or "Plasmoquine" irregularly. It is also found that cold weather or a debilitating illness may precipitate the disease. There is a well demonstrated association of the disease with malignant tertian malaria; but it appears that only certain strains of the parasite are likely to cause blackwater fever, and epidemics are known to have occurred amongst people who have not shown clinical signs of malaria. Manson-Bahr<sup>(2)</sup> comments on the work of Nocht, who believes that a hemolytic substance may be formed as a result of malarial infection, and that even when this is present in small quantities, it may cause a hemolytic crisis if it is associated with quinine. The exact nature of this hemolytic agent is subject to speculation. These conclusions appear to sum up modern opinion.

It is obvious, therefore, that no specific can be known for blackwater fever. Treatment is symptomatic, but is on well-established lines; the successful outcome of this case illustrates its value.

The aims of treatment must be: (i) careful nursing, (ii) prevention of renal failure, (iii) replacement of red cells, (iv) control of the malarial infection. These will be discussed in turn.

1. Devoted and expert nursing is essential. The patient must be kept warm and at complete rest; he must not be fatigued by transport from one place to another, even after the acute symptoms have subsided, for another hemolytic crisis may be initiated in this way.

2. Renal failure has often already commenced when the patient is first seen. It is caused by a mechanical plugging of urinary tubules by hemolytic products; this is less likely to occur if the reaction of the urine is alkaline and if large volumes are being passed. It was prevented in this case by frequent oral doses of alkali and by the fact that the patient was able to drink relatively large quantities of fluid. This latter was supplemented by the continuous intravenous administration of saline solution for two or three days. The fluid intake averaged about 100 ounces per day, and correspondingly large volumes of urine were excreted. The daily fluid balance is illustrated in Figure I.

3. Because of the severity of the hemolysis, evidenced by the massive excretion of blood pigment and the dramatic falls in the number of red cells discovered at successive blood counts, repeated blood transfusions are necessary. In this case, 5.5 litres of blood were given in a period of seven days. Although a life-saving procedure, blood transfusion carries the danger of reinstituting hemolysis by introducing slightly incompatible or fragile red cells, and in Papua there is the added danger of reinfecting the patient with malaria. An attempt was made to pick donors who had been on the island for only a short time and who had no history of febrile illness. Before each was used, a thick film of his blood was carefully searched for malarial parasites.

4. The control of the malarial infection is not of such immediate importance. Manson-Bahr states that "Atebrin" therapy should be commenced if parasites are found in the blood, so in this case treatment began on the first day. It has been shown that during the hemolytic crises of blackwater fever malarial parasites usually disappear from the peripheral blood, and that as a result the malaria is sometimes cured without further treatment. In other cases malaria may reappear later. Because of its known relationship to blackwater fever, quinine should not be employed, so it is usual to give a course of "Atebrin" and "Plasmoquine" after the patient has returned to health.

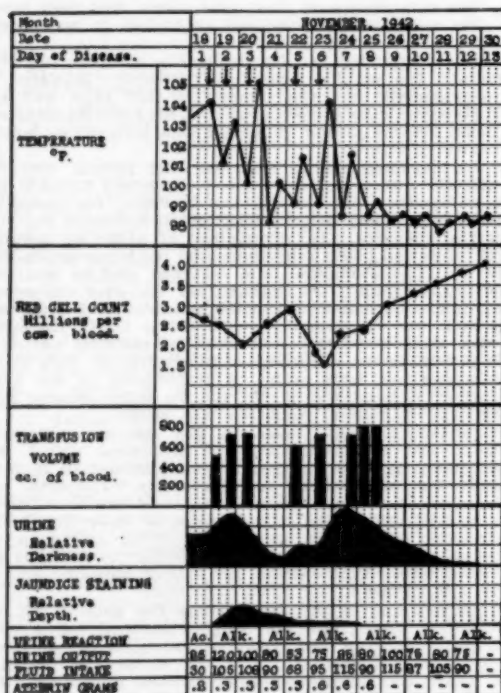


FIGURE I.

Diurnal temperature chart, graph of daily red cell count at ceters. The occurrence of a rigor is marked by an arrow at the top of the chart. The volume of blood given at each transfusion is represented in the corresponding day column by the length of the broad black line. The depth of coloration of the urine, which was a rough estimate of the daily rate of excretion of blood pigment, is shown graphically. At its highest point the graph line represents opaque, almost black urine. The depth of jaundice was estimated visually each day and is shown graphically. At its highest point, the graph line represents bright yellow staining of the skin. The daily dose of "Atebrin" in grammes and the daily total fluid intake and output in ounces are also recorded.

of the degree of hemolysis, and was a guide to the necessity for blood transfusions. In the first two days, the number of red cells fell by 600,000 per cubic millimetre, although 1,200 cubic centimetres of blood had been given. This probably meant that 1,600 or more cubic centimetres of blood had been hemolyzed. After a transfusion of 700 cubic centimetres on the third day, the expected rise of 500,000 red cells per cubic millimetre of blood occurred, and it was inferred that hemolysis had ceased. During the second series of hemolytic crises, the volume of blood hemolyzed again exceeded the transfusion volume; on the sixth day it was noted that the number of red cells fell from 1,800,000 to 1,500,000 per cubic millimetre during the course of a

### Summary.

The history is presented of the first case of blackwater fever encountered in an Australian military hospital in Papua, and comment is made on the clinical features and treatment of this disease.

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## Reviews.

### AN EPIC IN SALVAGE.

At midnight on June 18, 1940, the R.M.V. *Niagara* left Auckland harbour on her way to Vancouver. A little more than three hours later the war came violently to the southern hemisphere, for the *Niagara* struck an enemy mine and sank in 438 feet of water, carrying with her in particular £2,500,000 in gold ingots, which had been consigned by the Bank of England to the United States of America. The presence of the gold on board was known only to the master and to a few responsible persons; the whole transaction had been arranged with the utmost secrecy. Fortunately, all the passengers and crew were rescued. The fact that 94% of the gold was ultimately recovered is now common property; what is not so well known is the magnitude of the task involved in the salvage operations. James Taylor, a journalist who was present during the actual recovery of the gold, has written the history of the adventure—an adventure to stir the imagination of the most phlegmatic.<sup>1</sup> It is a story of the triumph of determination, of sound and intelligent planning, of unsurpassed leadership and of faultless teamwork over conditions that might have made the stoutest heart quail—lack of funds, perversity of the weather and sheer bad luck. The salvage ship *Claymore* was a veteran of forty years, who was retrieved from retirement on a mud bank and again put into commission to take on this work, which the leader of the expedition, Captain J. P. Williams, knew to be of national importance. After the gold had been recovered, *finis* was written to the life history of this honourable ship.

Much could be written of this epic undertaking, but it cannot be done in this place. However, mention must be made of one or two points of special interest. The first is the observation chamber used throughout the operations. It was specially designed by Mr. David Isaacs, of Melbourne, and constructed by the Thomson Engineering Works, of Castlemaine, and it incorporated all the best features of earlier observation chambers as well as some ideas of Captain Williams and Chief Diver Johnstone. It contained, amongst many other instruments, a barometer to register the internal pressure, which was increased to three and a half pounds above normal atmospheric pressure by the release of oxygen from a cylinder before the descent of the chamber. The occupant of the chamber wore a mask over his nose and mouth; when he exhaled, the carbon dioxide from his lungs passed through a container of soda lime and was absorbed—at least in theory. That the theory largely worked in practice is proved by the fact that the divers, the Johnstone brothers, were each able on many occasions to remain at wreck level for as long as four hours at a time. Such long spells were necessitated amongst other things by the position of the bullion room of the *Niagara*, in which the gold was stored, and by the fact that the diver had to direct by telephone the operations of the grab, which did the work, and which was worked from the *Claymore*. The diver could do nothing himself, and the fact that he could only give directions must have caused him much exasperation, notably on the occasion when the last ingot was known to be in what seemed a hopeless position, from which one false move of the grab would have dislodged it into eternal rest in the

mud. But an unexpected miracle happened, and the ingot was recovered. The resourcefulness of Captain Williams solved two important problems; the first was the "spinning" of the chamber due to the inevitable length of the suspending wire (which made the unfortunate diver as sick as the proverbial dog), and the second was the violent bumping of the chamber on the hull of the wreck, when the *Claymore* was plunging in a heavy sea, as she very frequently was. Thus, when the difficulties were overcome, the diver's life was made at least bearable. Taylor himself ultimately descended in the observation chamber to the wreck, and apart from the psychological effects of such a half-hour's adventure, he mentions no physical discomforts except a severe headache. It should be remembered that the operations were carried out at a much greater depth than any previous piece of salvage work.

Enough has been written to show the interest of this book. Let it be said in conclusion that James Taylor has done full justice to his subject, and that all who love adventure and applaud courage should read "Gold from the Sea".

### ENCEPHALITIS.

IN "Encephalitis: A Clinical Study" is presented the result of observations on some eight hundred cases of encephalitis, the continuation of a research begun by the Matheson Commission in 1918.<sup>1</sup> Dr. Josephine B. Neal describes the following varieties of encephalitis: epidemic encephalitis, St. Louis type encephalitis, Japanese B, human infection by the viruses of equine encephalomyelitis, verno-aestival tick-borne encephalitis, Australian X-disease, lymphocytic choriomeningitis, louping-ill, the Guillain-Barré syndrome, toxoplasmic and haemorrhagic encephalitis. Other contributors deal with neurological complications of acute infections and vaccination, the surgical treatment of post-encephalitic symptoms, psychiatric sequelae and pathology, to mention a few chapters.

The authors have been favourably impressed with the effect of a white wine decoction of Bulgarian belladonna in chronic encephalitis, but others have not had equally satisfactory results. Various belladonna and stramonium derivatives should be tried in the pre-pyramidal syndromes.

Should another visitation occur, this comprehensive book should be consulted for its wealth of information about the various aspects of the encephalitides. The numerous photomicrographs have been reproduced clearly and the general set-up of the book leaves little to be desired.

### A TEXT-BOOK OF MEDICINE.

THE heavy task of bringing the fourth edition of his text-book of medicine up to date, has been successfully accomplished by Dr. G. E. Beaumont, of the Middlesex and Brompton Hospitals.<sup>2</sup>

The volume of new material produced since the last edition six years ago has been such as to necessitate the writing of numerous new articles, and the rewriting of many others. The author has retained his original plan of including essentials only and omitting all extraneous matter, so that this edition is only twenty-six pages longer than its predecessor.

In spite of the difficulties and restrictions of wartime, the book is well produced, the paper good, and the print clear. Some of the new articles are very good, particularly those that are of special interest at the present time—for example, blast injury of the lungs and the crush syndrome. The poison gases also receive attention.

Among the new articles, reference may be made to descriptions of the following: *icterus gravis neonatorum* with erythroblastosis, prolapsed intervertebral disks, non-penetrating injuries of the heart, epidemic myalgia, the sulphonamide treatment of pneumonia, the aetiology of sciatica, uræmia, sex hormones, pneumonitis, sarcoidosis. The newer drugs that have proved their worth are all included, such as nicotinic acid, riboflavin, sulphadiazine, sulphaguanidine, heparin, stilbestrol and picrotoxin; also

<sup>1</sup> "Encephalitis: A Clinical Study", by Josephine B. Neal, A.B., M.D., Sc.D., F.A.C.P.; 1942. London: H. K. Lewis and Company, Limited. 9½" x 6", pp. 581, with illustrations. Price: 42s. net.

<sup>2</sup> "Medicine: Essentials for Practitioners and Students", by G. E. Beaumont, M.A., M.D., F.R.C.P., D.P.H.; Fourth Edition; 1942. London: J. and A. Churchill. 9½" x 6", pp. 818, with 71 illustrations. Price: 28s.

<sup>1</sup> "Gold from the Sea", by James Taylor; 1942. Sydney: Australasian Publishing Company, Proprietary, Limited. 8½" x 5½", pp. 271, with 17 illustrations. Price: 12s. 6d.

the more recently discovered vitamins. New diagnostic procedures mentioned are: sternal puncture, kymography, electro-encephalography and gastroscopy. The question of diet is not neglected, and many special diets are given.

The author's experience as a clinical teacher is reflected in some of his "clinical findings", notably in the section on diseases of the lungs, of which he has specialized knowledge. No man can be a specialist in every branch of medicine, and this fact has been used as an argument against the "one man" text-book such as this one; but as the author points out in his first preface, the general physician still has to look after patients suffering from most medical diseases, and has to instruct students in the symptoms, signs and treatment of such diseases. That it is impossible to compress modern medicine into 759 pages we all know, and much has to be omitted. For example, the student who relies entirely on this book, will find himself at a loss when confronted with a host of "functional" symptoms among his first private patients. Nevertheless, most of the "essentials" are here, and no doubt the book's popularity will increase with this up-to-date edition.

#### EXPERIMENTS AND STATISTICAL METHODS.

In the new edition of Professor Fisher's "The Design of Experiments", there is to be found only a little new material.<sup>1</sup> The numbering of the sections has not been changed and the new material introduced includes a fuller discussion of confounding and the treatment of completely orthogonal squares.

To the student of some standing in statistics, and especially to one who has had a thorough grounding in the author's companion volume "Statistical Methods for Research Workers", this new edition is an invaluable treatment of the uses to which statistics may be put. It is not a book for beginners, and while it possesses a definite agricultural bias, there is sufficient leaven of examples from other fields to indicate how biological and medical research could be strengthened by the use of modern statistical methods.

In the introductory chapters it is pointed out that the first problem in any experiment is the correct formulation of the question which the investigator is asking of the material. When the experiment is fairly simple, such as comparing the reactions of two homogeneous groups to a given set of conditions, fairly simple methods for evaluating the results are available. As one is often concerned with distinctly non-homogeneous populations and it is usually profitable to ask several questions simultaneously, experimental design and the methods used for interpreting the results become more and more complex.

It is with the analysis of variance and its various modifications that the rest of the book deals, different experimental designs being discussed. In the final chapters the author analyses the necessity for observing precision in experimentation and also the amount of useful information one may obtain from a given experimental arrangement.

#### SEX EDUCATION.

"PLAIN WORDS: A GUIDE TO SEX EDUCATION", by W. J. Thomas, should be read by all who may be called upon to advise the young, such as clergy, nurses, teachers and parents; it may safely be placed in the hands of adolescents for their guidance.<sup>2</sup> The information is couched in clear and concise language and for the most part is sound. Few will agree with the author's dictum that "knowledge" is the hand which sways the balance between normal happy sex expression and the abnormal and bestial: surely it should read "knowledge under the control of conscience". It is undoubted that knowledge unbridled by the inner voice of conscience may be more potent for evil than ignorance. Again it does not seem reasonable to acquiesce in the bald statement: "Sex hygiene ought to be a compulsory subject in every primary school." The author does not state just what he means by "sex hygiene"; some would include methods of contraception in this subject. Few primary

school teachers are competent either from theoretical or practical knowledge to take the responsibility of imparting knowledge on sex, and not many discerning parents would wish to hand this important subject over to teachers of whom they know nothing, whether those teachers are married or not. Undoubtedly biology should be taught as a science subject much more generally than it is; but the appalling ignorance amongst adolescents on sex will not be lessened until their parents have been properly instructed. The author passes some severe strictures upon the cowardice of politicians and the outmoded school of theological thought which is antagonistic to enlightenment upon sex matters. In his criticism of the Australian Broadcasting Commission and broadcasting generally, the author cannot have been aware of the broadcast upon social diseases given by the British Medical Association spokesman. A mistake requiring correction in subsequent editions occurs on page 30 where it is stated that the testicles remain in the abdominal cavity until puberty, whereas the descent begins during intra-uterine life, and in normal infants is completed by birth. The chapter upon human reproduction is excellent. The remarks upon continence and repression are sound, but there is no concrete suggestion as to how the large numbers of surplus women who because of monogamy are denied the normal expression of their maternal instincts shall deal with their problem. Obviously this difficulty will assume major proportions after the present war. It is to be regretted that the author has no chapter on suitable advice to be given to those about to marry. The chapter on venereal diseases is excellent, and the author insists that promiscuity is almost certain to lead ultimately to infection. This small book is a very valuable contribution to an important subject. The book is well set up and printed, and the illustrations are good and well suited for their purpose.

#### THE PASTEURIZATION OF MILK.

"THE PASTEURIZATION OF MILK", by Professor G. S. Wilson, is an excellent book from every point of view.<sup>1</sup> This is to be expected, for the author is a scientist of outstanding repute and an authority on bacteriology.

Much of the book can be easily understood by the lay mind, especially as the contents of each chapter are summarized in simple language. Clear explanations are given regarding the nutritive value of milk and the manner in which it may become infected with pathogenic organisms and thus become the vehicle for the spread of certain diseases. The influence of pasteurization is set out from every angle and objections to pasteurization are dispassionately discussed.

This is a book which should be read by all persons associated with the milk supply, including lay critics of modern methods, who often base their opinions on old-fashioned ideas or a scarcity of the complete facts.

#### ANTENATAL CARE.

SINCE many books have been published on antenatal care and allied subjects in the last few years, one which has attained its sixth edition is worthy of respect as having met a definite need in the community. Such is the case with the booklet by Professor F. J. Browne, of University College Hospital, London.<sup>3</sup> With his customary thoroughness, the author deals with all aspects of the pregnant woman's career, and he has included in this edition a chapter on the simple physiology of pregnancy and labour—a reasonable addition in these enlightened days. In some respects Professor Browne may be considered to have overdone the thoroughness of his advice. Detailed discussion of the toxemias of pregnancy appears to be excessive for the laywoman, and advice regarding the testing of urine seems likely to add to the burdens of the obstetrician. The details of clothing, and the scale of coupon requirements for the baby, are not applicable to Australian conditions. Otherwise the book is entirely satisfactory and should prove of great value to women, especially in their first pregnancy.

<sup>1</sup> "The Design of Experiments", by R. A. Fisher, Sc.D., F.R.S.; Third Edition; 1942. Edinburgh and London: Oliver and Boyd, Limited. 9" x 5½", pp. 248. Price: 12s. 6d. net.

<sup>2</sup> "Plain Words: A Guide to Sex Education", by W. J. Thomas, with forewords by Dr. H. E. Burghmann, Bishop of Goulburn, and Sir James Barrett, K.B.E., C.B., C.M.G., M.D.; 1942. Sydney: F. H. Johnston Publishing Company. 7½" x 4½", pp. 84, with illustrations. Price: 2s. 6d.

<sup>1</sup> "The Pasteurization of Milk", by G. S. Wilson, M.D., F.R.C.P., D.P.H., with a foreword by Sir Wilson Jameson, M.A., M.D., F.R.C.P., D.P.H., Hon. LL.D.; 1942. London: Edward Arnold and Company. 8½" x 5½", pp. 224. Price: 18s.

<sup>3</sup> "Advice to the Expectant Mother on the Care of Her Health and that of Her Child", by F. J. Browne, M.D., D.Sc., F.R.C.S.E., F.R.C.O.G.; Sixth Edition; 1942. Edinburgh: E. and S. Livingstone. 7½" x 4½", pp. 51. Price: 6d. net.



# The Medical Journal of Australia

SATURDAY, MAY 29, 1943.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: Initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

## THE HOSPITAL SHIP "CENTAUR".

By the time these words appear in the pages of the journal more than a week will have gone by since the sinking of His Majesty's Hospital Ship *Centaur* was announced to a horrified public. The news came as a heavy and unexpected blow. Horror gave way to anger, and anger to grief in the hearts of every Australian citizen. In the heat of war many deeds are done and have to be done because military necessity demands them, deeds from which men in other times would shrink. It is the knowledge of a righteous cause that makes it possible for men to do these things, a conviction that the future of the race and of humanity depends on them. This is one thing; but an attack on men and women dedicated to the relief of suffering and sailing under a badge known the world over as the mark of this service, is an action beyond the understanding of civilized peoples. It is of little use to fulminate against the foulness of the deed or the vileness of the men guilty of it. Those in authority must see that such steps are taken that a repetition of this thing will be impossible. For everyone in the community the occasion may be used to harden the resolve and steel the will to do what remains to be done. The medical profession mourns the loss of its members and of the nurses and other members of the Australian Army Medical Corps and of the Merchant Navy who perished with them. Appreciation of their sacrifice and the sacrifice of all those other members of the medical services who have given their lives in this war, must be shown by an increased devotion to the service of humanity at home and abroad, now and in the future.

## ANALGESIA IN OBSTETRICS.

To heal diseases and to relieve pain are unquestionably the noblest aims of the medical profession. While it seems that we shall never be able to attain our first goal completely, a great variety of means has been given into

our hands to achieve the latter. Nobody doubts that fullest use of the drugs at our disposal should be made in all diseases, except in very few cases in special circumstances, but ever since ether and chloroform were introduced and the opiates and barbiturates followed, one particular question has been asked again and again: "To what extent is one justified in using them to abolish childbirth pains?" The number of those who think that men should not interfere with the Creator's sentence "in sorrow thou shalt bring forth children", has become smaller and smaller; but on the other hand there is a group of honest men and women, amongst them not a few medical women with personal experience as mothers, who think that our endeavours to relieve Eve's daughters from the precept have gone a little far. It is not only that many children have paid with their lives for the relief the mother received; such events can largely be prevented by greater care and better judgement. Is it, however, right, they ask, that in some of the most efficient hospitals a general anaesthetic is administered as a routine procedure as early and for as long as possible, or that the woman is kept in a semi-conscious or unconscious condition by barbiturates *et cetera* until everything is over; that when she awakes, she is just told "It's a boy" and is often not allowed even to see, certainly to touch, her child for the next twenty-four hours? This certainly is right, when one regards mother and child just as a "case", or perhaps two cases, which have "to be dealt with" according to the most up-to-date rules and regulations. But are those really wrong who maintain that to obliterate the consciousness of a woman during delivery means to deprive her of one of the most profound and most beautiful emotional experiences, which will leave indelible traces on all her future life? Certainly, these traces should not be reminiscences of excruciating agony, but one should not forget that motherhood is more than a physical experience, more than an object for scientific procedures. A way out of this dilemma has been sought by many medical men and women. Local and spinal anaesthesia have been introduced, at least partly, for such reasons. Unfortunately, they are either not efficient enough or too dangerous. It seems, however, that a considerable advance in this direction has been made recently.

Robert A. Hingson and Waldo B. Edwards' report the results of a series of 589 cases in which a new type of anaesthesia was administered. The method, which they inaugurated some time ago and called "continuous caudal analgesia", is as follows. A special needle is introduced into the lower end of the sacral canal and placed into the intradural space. A rubber tube leads from the needle to a two-way adapter, which is connected with a syringe and a bottle containing the anaesthetic agent for which the authors recommend a 1.5% solution of methycaine. After carefully made tests (by aspiration) have shown that the needle has not entered the subarachnoid space, a trial dose of eight cubic centimetres is injected, and after ten minutes another thirty cubic centimetres are given. Supplementary injections of about twenty cubic centimetres are made every thirty to forty minutes during labour. The authors have continued injections up to thirty-three hours and for an average of seven hours. The average dose of methycaine was 2.6 grammes, the maximum dose 11.0 grammes. In a series of 100 cases

<sup>1</sup> The Journal of the American Medical Association, January 23, 1943.

in the authors' own hospitals there were only three unsatisfactory cases, in which some other anaesthesia became necessary. In the series of 489 cases, in which the authors managed or supervised the procedure in nineteen different medical schools and leading hospitals, the result was unsatisfactory in 11% of the cases. In many of these, however, the technique was practised by resident medical officers who were learning the procedure. In the entire series of 589 cases there were 586 living babies and no maternal complications or deaths.

Hingson and Edwards carefully set out in their paper indications and contraindications of the method, and so do Thomas G. Gready, junior, and H. Close Hesselstine in a short study of a small series, published in the same number of the journal. The main advantages of the new procedure seem to be the following. The anaesthesia is accurately controlled and may be continued for prolonged periods. It provides for the mother comfortable labour and painless delivery. The consciousness of the mother and the vital mechanisms of the child are not obtunded. The progress of labour and delivery is not interrupted; uterine contractions continue without impediment. The muscles of the abdominal wall and of the legs remain active, while those of the perineum are completely relaxed. Delivery and resuscitation of the child are expedited and facilitated. The systemic well-being of the mother is not endangered. Post-delivery complications are reduced. Disadvantages are that the technique is not easy, the greatest danger being that the needle enters the subarachnoid space, that anatomical variations of the lower end of the sacral canal may make the method impracticable, and that the procedure requires the presence of a specially trained anaesthetist throughout labour.

Impressed by the result of these studies, the editor of *The Journal of the American Medical Association* has invited the comment of some of the leading American obstetricians and publishes some replies he received in the same issue. N. W. Vause, Professor of Obstetrics at Jefferson Medical College, states: "It is a 100 per cent. effective analgesia and is not dangerous if properly administered. There are a few contraindications to its use, chief of which is *placenta praevia*. The labour is definitely shortened. Cervical dilatation is more rapid. Postpartum blood loss is less. Primary respiration in the infant is established promptly. Involution of the uterus is hastened. This form of analgesia does not inhibit or delay lactation. Bladder function is not disturbed. There is no lower extremity paralysis. Our time has been limited in the use of this method, but our results so far show that it is the best method yet devised for the relief of pain in labour."

F. R. Irving, associate Professor of Obstetrics at Syracuse, New York, first discusses some difficulties in the technical procedure and the possibility of adverse effects of the position of the mother on the foetal heart, but then states that with these points receiving due consideration, the method seems to be "the last word in obstetric analgesia". J. S. Lundy, head of the Department of Anesthesia in the Mayo Clinic, says of the method: "I think it is fine."

The excellent results reported in the two papers and the enthusiastic comments by three leading obstetricians are impressive enough to warrant the suggestion that a fair trial should be given to the method, wherever proper

facilities for its administration exist. It may be stressed again: that the method is not yet one for general practice; that it should be reserved for the time being for the large hospitals; that the cooperation of an anaesthetist, very well versed in spinal anaesthesia, is necessary. It may be mentioned that Hingson and Edwards made themselves thoroughly familiar with the technique by trying it on twenty cadavers before they first used it in the treatment of a patient. The results seem to be so favourable, from the physical as well as from the psychological point of view, that anyone prepared to do all the necessary spade work should find ample compensation.

## Current Comment.

### SULPHADIAZINE.

SOME little time has now elapsed since reports first reached this country of the virtues of sulphadiazine and of its alleged superiority over other drugs of the sulphonamide series. Perhaps it has not been altogether a disadvantage that supplies of the drug have not been readily available in Australia, for this has prevented the over-enthusiastic rush to use it that is so often seen when a drug or other clinical remedy is loudly proclaimed in medical literature. In any discussion on the sulphonamide drugs at the present time, it is necessary to point out more than once that desire to use them must be tempered by their availability. Relatively large stocks of other sulphonamide drugs have been available in Australia, and for this reason over-enthusiasm for sulphadiazine has quite rightly been discouraged by the Medical Equipment Control Committee of the Commonwealth. Many interesting claims have been made in regard to the effectiveness of sulphadiazine, and reports of toxic effects caused by it have been published from time to time. It is appropriate that attention should be drawn to some of the more recent communications. Before any of these are mentioned, it is well to point out that a report was made on this drug in May, 1941, for the Council on Pharmacy and Chemistry of the American Medical Association by Perrin H. Long.<sup>1</sup>

Long confirmed the observations of Feinstein and his associates published in December, 1940, that the blood concentrations following administration of the drug to mice were about four times as high as those resulting from comparable doses of sulphapyridine or sulphathiazole, and that the drug existed in the blood primarily in the free form because the acetyl derivative appeared to be readily excreted in the urine. They also confirmed the observation that sulphadiazine produced less tissue damage in mice than sulphathiazole or sulphapyridine. At the same time, Long and his associates, unlike Plummer and Ensworth, found that the drug was somewhat less readily absorbed from the gastro-intestinal tract than were sulphanilamide, sulphapyridine and sulphathiazole. They also stated the tentative conclusion that sulphadiazine passed over into the spinal fluid in concentrations of from two-thirds to four-fifths of those which existed in the blood. When Long wrote, he thought that it was too early to make a definite statement regarding the relative clinical therapeutic merits of sulphadiazine, sulphanilamide, sulphapyridine and sulphathiazole. He thought that the evaluation of sulphadiazine would necessitate extensive experimental and clinical investigations. "Until the time when such data are available", he wrote, "it is to be hoped that preliminary enthusiasms will not outrun the common sense which we have gained as a result of our experiences with sulfanilamide and its other derivatives during the past five years."

<sup>1</sup> *The Journal of the American Medical Association*, May 24, 1941, page 2399.

In 1941 M. Finland, O. L. Peterson and E. Strauss reported on the use of sulphadiazine in the treatment of 446 patients suffering from pneumococcal, staphylococcal and streptococcal conditions. Finland and Peterson, with R. A. Goodwin, have now reported clinical studies of the efficacy and toxic effects of sulphadiazine in the treatment of 460 patients.<sup>1</sup> None of these were included in the report of 1941. The previous findings have been confirmed and they now think that sulphadiazine is to be preferred in infections due to hæmolytic streptococci and in the various forms of acute bacterial meningitis. They find that in acute gonococcal and staphylococcal infections and in acute infections of the urinary tract, the efficacy of sulphadiazine is probably similar to that of sulphathiazole. On account of its lower toxicity, however, they think that it is to be preferred to sulphathiazole, particularly when prolonged therapy is desirable. From their own results and from those reported by others, Finland, Peterson and Goodwin think that there is justification for the claim that sulphadiazine is the most suitable sulphonamide for initiating chemotherapy in all acute pulmonary infections, and for continuing treatment in such conditions when they are caused by the pneumococcus, the streptococcus and probably also the staphylococcus and Friedländer's bacillus. Though toxic effects were relatively few and mild, Finland and his fellow workers point out that the comparatively frequent occurrence of complications in the urinary tract calls for the exercise of caution in the control of the dosage of the drug in relation to fluid intake and output. This is particularly necessary in the treatment of old persons, of patients with hypertension and of those who may have some impairment of renal function. With adequate control, however, it is held that the drug may be administered so as to produce therapeutically effective blood levels whenever they are indicated, even in the presence of severe renal disease. When oliguria occurs the fluid intake should be promptly increased or the dose of the drug reduced. If pronounced or complete suppression of urine occurs, particularly if it is accompanied by ureteral pain, large quantities of fluid should be given and ureteral catheterization should be employed early if a fatal outcome is to be avoided.

One of the patients in the series described by Finland, Peterson and Goodwin died "presumably of a renal complication". In this instance a woman eighty-four years of age was treated with sulphadiazine for erysipelas. Symptoms suggestive of right ureteral colic were followed by diminution in the urinary output, and the urine was found to contain red blood cells and crystals. The patient died in spite of suitable treatment.

In a paper on the renal complications caused by sulphadiazine, D. O. Wright and R. E. Kinsey, of the United States Army,<sup>2</sup> draw attention to the importance of hæmaturia as a sign of impending trouble when sulphadiazine is being administered. They think that the appearance of even a few blood cells in the urine should be looked on as a warning sign. No less than seven of 38 patients to whom sulphadiazine was given suffered from renal complications. Wright and Kinsey observed that the average daily output of urine was low in comparison to the intake of fluid. Though this was partly accounted for by the fact that the patients were being treated in a torrid climate, this low output was the only constant finding in the seven cases prior to the onset of hæmaturia. In making this observation, Wright and Kinsey point out that low urinary output cannot be considered as the only causative factor because cases of renal irritation have been reported in which the urinary output was not unusually low. A constant finding in all seven instances was renal tenderness, and in two cases it was present six hours before hæmaturia occurred. Wright and Kinsey refer to observations by Hellwig and Reed and by Keltzer and Campbell, published in June, 1942, that renal lesions caused by this drug are of two kinds. One type of lesion may be the result of mechanical blocking of the urinary passages, and the other a toxic effect on the tubular

epithelium similar to the type of lesion found in mercury poisoning. Wright and Kinsey conclude that the finding of even a few red blood cells, with or without crystals, in the urine is an indication that the drug should be withdrawn. Their views are supported by A. L. Louria and C. Solomon, who report a case of complete anuria caused by sulphadiazine.<sup>3</sup> As a matter of fact, these observers draw attention to the rarity of renal complications with sulphadiazine, and explain it by the observations of Feinstein and his colleagues, first, that the solubility of acetyl sulphadiazine in the urine is much higher than that of the acetyl derivatives of sulphapyridine and sulphathiazole, and secondly, that sulphadiazine is not conjugated to the same extent as sulphapyridine. The anuria of Louria and Solomon's patient was due to mechanical blocking, and no hæmaturia was noticed. The patient recovered after ureteral catheterization. From the literature and from their own observations, these two workers conclude that if the urinary output is good, the presence of crystals in the voided urine should not be considered as an indication for discontinuing the drug. At the same time, they think that the drug should be discontinued if gross blood appears in the urine at any time. They state that hæmaturia clears up promptly after the drug has been stopped, and add that no permanent renal damage has been observed in the cases in which recovery has occurred.

The last paper to which attention should be drawn is one by W. D. Sutliff, N. Helpert, G. Gritting, and H. Brown, who discuss sulphonamide toxicity as a cause of death in New York city in 1941.<sup>4</sup> During that year, 28 deaths were caused by sulphonamides. In three of these cases, sulphadiazine was used. In two cases, the toxicity affected the kidney, and in the third the blood cells and blood-forming organs were involved, thrombocytopenic purpura occurring. Sutliff and his collaborators raise the question of the reduction of dosage of sulphonamides and state that it is not advisable to change standard dosage schedules which are known to be successful, since they are based on experimental demonstrations of the need for certain minimum blood levels of the drugs in order that a maximum therapeutic effect may be produced. The steps that should be taken on the appearance of toxic symptoms will be clear from what has been written above. One point mentioned by Sutliff and his co-workers is that the urine should be made alkaline in the presence of hæmoglobin nephrosis. In this regard Louria and Solomon state that it is still a moot point whether alkalization of the urine will deter crystal deposition in the urinary tract. The general conclusion reached by Sutliff and his co-workers is that there is no evidence that would justify modification of the course that is being pursued in the routine use and in the experimental extension of the use of sulphonamide drugs. They state that the benefits derived from this course are much greater than the risk of serious toxic reaction incurred. In the discussion that followed the reading of the paper, R. L. Cecil concluded with the common-sense remark that perhaps the surest way to avoid fatal toxic reactions was to use the minimum amount of drug necessary to control the infection. Another point that should be emphasized has to do with the duration of treatment. Reference has not been made in this discussion to the occurrence of granulocytopenia, a rarer event than involvement of the renal tract. (Among the 460 patients reported by Finland, Peterson and Goodwin there was only one who manifested complete absence of granulocytes.) Perrin H. Long pointed out that the time factor was important and that granulocytopenia occurred with few exceptions after the twelfth day of treatment. Some idea of the vogue for the use of sulphonamides may be gathered from Long's statement that in 1941 somewhere in the neighbourhood of ten to fifteen million persons in the United States received one of the sulphonamide derivatives. There is surely abundant evidence for the contention that doctors should study chemotherapy in all its aspects.

<sup>1</sup> *Annals of Internal Medicine*, December, 1942.

<sup>2</sup> *The Journal of the American Medical Association*, December 26, 1942.

<sup>3</sup> *The Journal of the American Medical Association*, December 26, 1942.

<sup>4</sup> *The Journal of the American Medical Association*, January 30, 1943.



## Abstracts from Medical Literature.

### OPHTHALMOLOGY.

#### Cholesterin and Fat Deposition in Mustard Gas Injuries of the Cornea.

IDA MANN AND B. D. PULLINGER (*The British Journal of Ophthalmology*, November, 1942) state that the series of changes that precede the onset of delayed mustard gas ulceration of the cornea lead to the deposition of fat and cholesterin in the *substantia propria*. This degeneration is known to occur also as a sequel to severe keratitis, either infective or brought about by such chemicals as sulphuric acid. Using rabbits, the authors produced cholesterin-containing scars in 14 eyes out of a total of 125 possible experiments. The mechanism of production is still somewhat obscure. They found that (i) central corneal lesions healed without vascularization of the cornea and (ii) such avascular lesions never produced cholesterin or fat in the scars. The authors therefore conclude that previous vascularization of the cornea is the essential factor in this degeneration. They state that this vascularization is of various types, which they describe in some detail. In attempting to assess the probability that cholesterin would be formed in any given case, they made the discovery that in the series of eyes that received treatment for the mustard gas injuries, a much higher percentage of degenerate scars occurred than in the series in which the lesion was allowed to run its usual self-limiting course. Forty eyes were treated in various ways (by irrigations of tap water and saline solution, or by the instillation of drops of liquid paraffin, glycerine, "Albucid", bleach solution, sodium bicarbonate, cod liver oil alone or in combination with sodium bicarbonate, or Bonnefont's solution), and in eight of these cholesterin scars developed; of 85 untreated eyes, cholesterin scars developed in six. It is possible that continued damage after the initial injury influences the production of these scars. The lipid occurs in two forms: (i) as very fine droplets, like an emulsion bathing the fibrils of the *substantia propria*, and (ii) as large intracellular globules and crystals having the characters of esters of cholesterin. The history of these scars throws some light on the pathology of atheroma. The authors believe, from their observations on the cornea, that a hypothetical substance or substances, "X", may, in the first place by reaching the intima, or if the substance is a vitamin by failing to reach it, cause sufficient damage to bring in capillaries as part of an inflammatory reaction. This vascularization, common in atheroma, may be followed by regression and by deposition of lipid. They admit that their theory is pure speculation, but hold that it does not disagree with the facts.

#### Epidemic Kerato-Conjunctivitis.

M. SANDERS, F. D. GULLIVER, L. L. FORCHHEIMER AND R. C. ALEXANDER (*The Journal of the American Medical Association*, January 23, 1943) have investigated from the clinical, epidemio-

logical and experimental aspects 80 patients suffering from epidemic kerato-conjunctivitis. Significant diagnostic features in all cases were hyperæmia and swelling of the palpebral conjunctiva, congestion and hyperæmia of the bulbar conjunctiva, oedema of the lids, the occasional occurrence of pseudomembranes on the conjunctiva of the lower lid, lymph node involvement and absence of discharge. Corneal involvement was present in 42 cases; no absorption of corneal opacities had taken place after five months, and 14 of the 42 patients had impairment of vision ranging from 5% to 15%. Associated systemic symptoms were headache (49 cases) and malaise (26 cases). In three cases the ocular disease was mild and the systemic symptoms were severe. In all cases, when the ocular disease was severe, systemic symptoms were present. Fifty-seven patients were absent from work for periods varying from one to eight weeks. Individual predisposing factors to the disease appeared to be present, but the nature of these factors is not fully understood; 70 of the 80 patients contracted the disease after ocular trauma or inflammation. By cultural methods, in two of nine attempts a filterable virus was obtained, which appeared to be identical with that isolated in an earlier investigation of the condition. The virus produced symptoms in mice, and was neutralized by convalescent serum from a patient suffering from the disease, but unconnected with the series under review. In six of nineteen specimens of serum from convalescent patients, antibody development was demonstrated. Specimens of serum taken soon after the onset of the disease were compared with specimens taken from 17 to 34 days afterwards; in all cases there was a distinct increase in the antibody titres of the second samples. This indicates a specific relationship between the virus and epidemic kerato-conjunctivitis.

#### Granuloma Inguinale of the Eyelid.

A. L. WEINER, I. E. GAYNON AND M. S. OSHERWITZ (*American Journal of Ophthalmology*, January, 1943) record a case of *granuloma inguinale* of the eyelid following *granuloma inguinale* of the penis. The patient was a Negro, who was admitted to hospital with a urological history and symptoms that caused him to be treated immediately for urethral stricture with urinary retention and extravasation. Both medical and surgical treatment were given. There was no suggestion of syphilis, and no syphilitic treatment was undertaken. During his stay in hospital, the patient's blood reacted to the Kahn test. One month later ophthalmological examination was required for recurrent styes. The chief abnormality detected was what appeared to be an acute hordeolum in the left upper lid; it was the size of a large pea and was beginning to point at the base of the cilia. Treatment by incision and the application of sodium sulphathiazole ointment (5%) and hot compresses was begun. Pus from the lesion yielded a growth of *Staphylococcus aureus*. Two weeks later examination revealed extensive necrotizing ulceration of the middle half of the left upper lid; a large crescentic area, including a large portion of the tarsus, had sloughed away. The margins of the ulcer were irregular,

and the surface was covered by a profuse, dirty grey discharge. There was little pain or tenderness. A section of tissue was histologically examined, and a diagnosis of acute and chronic inflammation of the eyelid was made. Treatment was changed to the application of a 2% solution of silver nitrate, and the patient was advised to continue the use of sodium sulphathiazole ointment and hot compresses; but there was no appreciable response to this therapy. The patient was then investigated for syphilis, with negative results. The Frei test for *lymphogranuloma inguinale* produced no reaction. The diagnosis was then revised; it was considered that the destructive lesion of the eyelid might be an extension of the *granuloma inguinale* from which the patient was known to have suffered approximately six weeks previously. The original histological sections were reexamined, and the characteristic large monocytes containing Donovan bodies were found. Most of the inflammatory cells were polymorphonuclear leucocytes. Treatment with bi-weekly injections of tartar emetic (ten cubic centimetres of a 1% solution) was begun, and the eyelid healed completely within six weeks. The treatment was continued for several months, to offset the tendency to relapse. The authors point out that the clinical aspects of the ulcer of the eyelid were characteristic of *granuloma inguinale* in other situations; it began as a hard, oedematous area and progressed to ulceration and destruction of tissue. The histological findings and the prompt response to tartar emetic therapy were also characteristic. If the patient had been given anti-syphilitic treatment on account of the fact that his blood reacted to the Kahn test, the true diagnosis would have been obscured or lost, since the arsphenamines exert a beneficial therapeutic action upon the lesions of *granuloma inguinale*; but tartar emetic is of no value in syphilitic lesions.

#### Ocular Findings in Children with Endocrine Disorders.

CARL APPLE AND I. P. BRONSTEIN (*American Journal of Ophthalmology*, January, 1943) present the results of an ophthalmological study of 108 children with various endocrine disorders. The children were grouped as follows: 63 were obese and were referred as suffering from Frölich's syndrome, 17 were of less than normal stature (presumably from pituitary abnormality), eight were hypothyroid, and ten formed a heterogeneous group (three had hypogonadism, two had gigantism, three were sexually precocious and two showed signs of pseudohermaphroditism). The authors first discuss the various groups in some detail. They remark that recent work by others as well as themselves has emphasized the fallacy of designating the much overweight child as suffering from Frölich's syndrome, which is a rarity; the suggestion has been made that the term should be deleted from the literature. They believe that neither pituitary nor thyroid disease need be postulated; the obesity tends to correct itself at or about puberty, when mentally adequate children recognize their obesity as a handicap and become willing to cooperate in a dietary régime. The ocular findings amongst the obese children were no different from those in any group of

normal children. Amongst children of less than normal stature, the ocular findings did not differ from those in any normal group. There was no evidence of visual disturbances from presumably altered secretions of the pituitary gland. The visual acuity of the children in the hypothyroid group was below normal; six of them were hyperopic and six had more than two diopters of refractive error; only one of the eight was myopic. In the remaining ten children, comprising the heterogeneous group, no ocular abnormalities were found. The altered secretions causing the various abnormalities apparently have no effect upon the eyes.

### OTO-RHINO-LARYNGOLOGY.

#### Sulphadiazine and Mastoidectomy.

A. TUCKER AND C. G. FLAKE (*The New England Journal of Medicine*, December 31, 1942) discuss the use of sulphadiazine in the management of simple mastoidectomy wounds. A series of cases from a children's hospital was divided into three groups. In the first group the mastoid cavity was filled with sulphadiazine powder and the wound completely sutured, while none of the drug was given internally. In the next group no local application of the drug was made, but the patients received oral chemotherapy for one day before operation and for seven to ten days after operation, a blood concentration of 10 to 15 milligrammes per 100 cubic centimetres being aimed at. In this group also the wound was sutured completely. In the third group chemotherapy was omitted entirely both from the wound and by oral administration; the wound, however, was drained from its lower angle. In the group receiving local chemotherapy primary healing occurred in all and aural discharge ceased after an average of ten days. In those treated by oral administration only, primary healing occurred in all but two of fifteen cases and discharge from the ear ceased after 8.2 days. In the group from which all chemotherapy was withheld healing took up to three weeks to occur and aural discharge lasted up to fifteen days. The authors conclude that the patients receiving chemotherapy fared about equally as well whether treated locally or by mouth. Healing of the wound was improved when the drug was used locally. Patients receiving no chemotherapy had a much longer convalescence and healing of the wound took considerably longer.

#### Progressive Middle Ear Deafness.

I. SIMPSON HALL (*Edinburgh Medical Journal*, June, 1942) discusses progressive middle ear deafness. He grades cases into catarrhal conditions, middle ear suppuration and otosclerosis. The first group principally occurs in children and can be cured, if found early in the systematic examination of school children, by removal of tonsils and adenoids, by correction of sinus disease and by Eustachian inflation. In cases of middle ear suppuration, those patients who respond to simple mastoidectomy usually obtain good functional results. It is in the more chronic group, which require direct drainage of the middle ear and eradication of established foci of bony disease,

that more thought has been given to the forms of operating and after-care which aim at conservation of function. The author refers to the series of cases reported by the late J. S. Fraser in 1930, in which, of 499 operations, 401 were by the radical method, and in only 98 was the more conservative modified radical mastoidectomy employed. Reviewing the more recent experience in his department, the author reports a series of 500 cases occurring in patients who were carefully followed up. Two hundred and sixty-one of these underwent a modified operation and 239 were treated by the radical method. In the author's own personal experience, of 373 operations, 211 were of the modified type and 162 were radical, the percentage of successful results as indicated by a dry ear being 95 and 85 respectively. Stress is laid upon after treatment, whatever method is employed. Personal care by one specially trained for up to nine weeks is considered essential. Of a variety of methods of treating the wound cavity, secondary skin grafting, after a granulating surface has been allowed to form, was most satisfactory. Primary grafting at the time of operation has been abandoned in the author's practice. In cases of otosclerosis, some hope is expressed for endocrine therapy. Attempts to give relief from deafness by labyrinthine fenestration have been made in 31 cases, ten patients showing improvement, ten being unchanged and one worse. In no instance did labyrinthine infection supervene. Some hope is expressed that amnioplastin may be of value towards preventing endolabyrinthine adhesions and so avoiding one of the reasons for failure to maintain improvement.

#### Otitis Media and Mastoiditis in Children.

A. G. DE SANCTIS, V. P. LARKIN AND W. A. GUGLEMAN (*The Journal of the American Medical Association*, November 14, 1942) have made a critical study of 1,992 cases of otitis media and mastoiditis occurring in patients admitted during the years 1931 to 1941 to the New York Post-Graduate Hospital. By a process of dissection of symptoms and percentage comparisons of each, it appears to be established that there has been no decrease in the severity of otitis media and mastoiditis during the period under review. Not only is there shown to have been a marked decrease in the incidence of otitis media in the last four years of the survey period, but the development of mastoiditis has dropped in relation to the total number of cases from one in less than three during the earlier years to one in fifteen in 1941. There was a decided increase in the number of cases of scarlet fever in 1941, yet fewer cases of otitis media were recorded. Myringotomy was performed in between 50% and 60% of cases prior to 1936, but the operation has been performed very much less frequently since 1936 and was resorted to in only 10% of the cases in 1941. It was during the latter six-year period that sulphonamides were used so often that in 1941 they were exhibited in nearly 100% of all cases. In spite of this avoidance of routine surgical drainage the incidence of mastoiditis and other complications has been reduced to only one in fifteen cases. The authors conclude that to chemotherapy alone is

this change in outlook attributable. Throughout the survey period bacterial cultures have been made. The hæmolytic streptococcus was the commonest organism occurring in pure culture, next the *Staphylococcus aureus* and then pneumococci. The streptococcus was found alone in 80% of cases in which mastoiditis developed. Sulphathiazole was found to be the therapeutic agent of choice. One grain per pound of body weight, per day, is the recommended dosage. Treatment with full dosage is continued for four days after the temperature has returned to normal, or for two days after cessation of discharge, when present. Daily examination of the urine and examination of the blood every second day are recommended.

#### Bronchoscopy in the Diagnosis and Treatment of Bronchiectasis in Children.

D. E. S. WISHART (*The Journal of the American Medical Association*, December 12, 1942) discusses the routine which has been devised after the treatment of some of 430 children suffering from bronchiectasis at the Hospital for Sick Children in Toronto during the past thirteen years. Diagnosis was established in 230 of these cases by contrast medium radiograph, iodized oil being placed into the lungs directly through the bronchoscope. The examinations are carried out on a specially devised table which permits X-ray screening to be used and films to be speedily changed so that pictures are able to be taken as various parts of the lung are injected with the oil. General anaesthesia is employed. Sedative premedication, though used in the earlier years, is now omitted as it is felt that an active cough reflex assists the procedure. While suction cleaning is being carried out light anaesthesia is maintained in order that the coughing reflex may aid the process; then when the oil is to be injected anaesthesia is deepened and so maintained for about five minutes while in the now darkened room the fluorescent screen is employed to determine when sufficient oil has been used to fill the particular lobe about which information is sought. When finally the screening reveals that adequate filling of the selected area has been achieved two antero-posterior and two lateral films are taken. Overfilling with oil, which may be brought about by using a tube which too tightly fits a bronchus or by too rapid injection of the oil, may produce inaccurate and misleading films. With some serial bronchograms from individual patients, made at different stages during the course of suction treatments, the author stresses the more revealing accuracy of detail to be obtained after a period of treatment and after more painstaking efforts to clean out the bronchi thoroughly. Complications have been rare. Laryngeal oedema which was encountered after instrumentation in the very young has been eliminated by always using a fine bronchoscope, never larger than five millimetres in bore. In one child, the use of oil, before profuse secretion had been overcome by drainage and suction treatments, appeared to cause a great increase of secretion, so that the patient died in spite of all efforts to reduce the exudate by aspiration. Children under one year of age are considered unsuitable for contrast medium bronchography.

## Medical Societies.

### THE MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA.

A MEETING of the Medical Sciences Club of South Australia was held at the Institute of Medical and Veterinary Science, Adelaide, on June 5, 1942.

#### Adelaide Health Survey.

Dr. H. K. Fry gave a short history of the establishment of the X-ray health survey by the Adelaide Local Board of Health.

During March, attendances reached a total of 10,000, which was considered a sufficient number to make a statistical analysis of some value. This analysis demonstrated a percentage of abnormalities warranting further investigation ranging from 2% in young children to as high as 25% in late years of life. At each age abnormalities in males exceeded those in females.

Of these abnormalities, those reported as probably or possibly tuberculosis by the radiologists were grouped and found to be roughly about half the number of total abnormalities, except that in the older male age groups this proportion was greatly exceeded. This was a finding of great importance in the epidemiology of pulmonary tuberculosis. The results of the survey were also grouped in regard to the history given by the patient. Those giving a significant history of illness and those giving no such history were considered separately. The latter showed a percentage of abnormalities roughly half that of the former, except in the older age groups of both males and females in which the proportion was higher. Graphs were exhibited demonstrating these findings.

The value of mass X-ray examinations of the chest in the absence or slightness of symptoms accompanying early infection, and the difficulty or impossibility of detecting signs of infection by clinical examination were discussed.

#### The "Staggers" Syndrome.

Mr. I. W. McDonald presented a paper entitled "The 'Staggers' Syndrome in Domestic Animals, with Special Reference to a New Type Observed in South Australia and Associated with the Ingestion of *Phalaris tuberosa*". He said that the term "staggers" was used colloquially to describe a wide variety of diseases in domestic animals, in which muscular incoordination was the prominent feature of the symptoms. The etiological factors were numerous and varied. The term "staggers syndrome" had been applied to a group of diseases with the following characters: They were caused by ingestion of certain "toxic" plants, almost invariably under grazing conditions which forced animals to consume a diet wholly or chiefly composed of the plant in question. Usually only a few days or weeks of grazing on the plant were sufficient to produce symptoms. Affected animals might appear normal while grazing quietly, but symptoms were readily elicited or intensified by excitement or driving. The chief symptoms were incoordination and tremor. The animal might fall and struggle vigorously but ineffectually to rise to his feet. After a short period of rest, the nervous condition improved and symptoms might even disappear, only to reappear if the exciting influence was renewed. Forced exercise produced rapid exhaustion and even death. Recovery usually occurred within a few days after removal from the toxic pasture. No pathogenic lesions were observed at autopsy.

At least twelve species of plants were known as causal agents. In South Australia, staggers had been observed in sheep and cattle and were due to grazing on *Phalaris tuberosa*. This disease resembled closely that due to the ingestion of perennial rye grass (*Lolium perenne*). Pathological changes had been observed in the central nervous system and in the kidney. The pathogenesis of the disease was obscure. The evidence available suggested that the disease occurred only when *Phalaris* was grown on soils which were deficient in some essential elements.

A MEETING of the Medical Sciences Club of South Australia was held at the Institute of Medical and Veterinary Science, Adelaide, on July 3, 1942.

#### The Drying of Human Serum Proteins.

Dr. J. Funder presented a paper on the drying of human serum proteins. He said that the advantages of preparing human serum in the dry form were that, in this form, the serum might be preserved at ordinary room temperatures for a long period without any appreciable denaturation of the serum proteins and consequent loss of the biological properties associated with the serum proteins. Further, serum in the dry form did not present a favourable medium for the growth of any chance contaminating organisms, and possessed the advantage that it readily lent itself to the preparation of protein solutions of varying concentrations for clinical use.

In most large-scale methods of production of dried serum drying *in vacuo* of serum which had been frozen prior to its admission by the desiccating chamber was employed, the condensate being collected either by chemical desiccants, or as ice on refrigerated surfaces, coils, maintained at a temperature of  $-40^{\circ}$  C. or lower. Recently processes had been devised in which liquid serum was admitted into the desiccating chamber in the form of a very fine spray, and the drying of this spray was done by a stream of hot sterile air admitted from the periphery of the desiccating cylinder. These processes—involving drying from the liquid state—had not as yet, however, become as firmly established as processes involving the drying of pre-frozen serum. The process used in Adelaide for the past year was that developed by Greaves and Adair, of the Department of Pathology, Cambridge University. Its main features were the use of refrigerator coils, maintained at  $-40^{\circ}$  to  $-50^{\circ}$  C., as condenser for the water vapour, precise thermostatic control of the amount of heat to which the serum was subjected during drying, continuous recording of the temperature of the drying serum and the refrigerator coil throughout the three-day main drying cycle, and final desiccation for three days, phosphorus pentoxide being used as desiccant.

#### The Delayed Development in Grasshopper Eggs.

Mr. H. G. Andrewartha presented a paper on delayed development (diapause) in grasshopper eggs. He said that the term "diapause" had been coined by Wheeler in 1893 to describe a stage in the embryonic development of a grasshopper *Concepthalus*. In 1869 Duclaux had shown that the eggs of certain univoltine races of silkworm (*Bombyx*) did not hatch if they were kept continuously in a warm room. But if they were exposed to open air temperatures during the winter they were able to complete their development in the spring. In 1904, Henneguy used the term diapause to describe the state of arrested development which was known to occur in the eggs of *Bombyx* and the larvae of *Liparis*.

It was in Henneguy's sense that the word had been accepted by modern authors. Some confusion had been introduced by certain modern workers who had failed to distinguish between simple "cold-dormancy" and the more complicated phenomenon of diapause which occurred, for example, in the eggs of *Austroicetes* and the larva of *Platyedra*. In the former case development would be resumed when the organism was returned to a favourable high temperature; in the latter case development might not be resumed until diapause had been eliminated by some suitable treatment.

A complex factorial experiment had been made with the eggs of *Austroicetes cruciata*, three variables being used, namely, temperature, duration of exposure to temperature and stage of embryo. From the results of this experiment and from observations on the abnormal development of embryos in the artificial conditions of the experiment, the following conclusions were reached:

1. Diapause occurred because the yolk was in an unfavourable condition for the normal growth of the embryo. The elimination of diapause from the egg was associated with certain changes in the yolk, which proceeded at "low" temperatures.

2. The processes associated with the elimination of diapause were different from those associated with the growth of the embryo. The former were most rapid at about  $10^{\circ}$  C.; they were active as low as  $60^{\circ}$  C. and up to about  $13^{\circ}$  C. The latter were most rapid at about  $30^{\circ}$  C.; they were too slow to be measured at temperatures below  $13^{\circ}$  C.

3. Diapause was not completely eliminated from eggs unless the exposure to low temperatures occurred when the embryo was at a suitable stage of development.

This meant that in nature *Austroicetes cruciata* could persist only in those areas in which it was delicately in



tune with the environment. This restricted the insect to a particular climatic zone. It also ensured that the active stages of the insect would be about at the one period of the year when green feed was likely to be abundant.

Knowledge of the phenomenon of diapause was of fundamental importance to the ecologist, since it provided the clue to many problems associated with the relationship of the physical environment to the distribution and abundance of insects.

## The Royal Australasian College of Physicians.

### ANNUAL MEETING.

THE fifth annual meeting of the Royal Australasian College of Physicians was held at Melbourne in the building of the Royal Australasian College of Surgeons on Thursday, Friday and Saturday, April 8, 9 and 10, 1943. Meetings of the Council, the Board of Censors, general meetings and a scientific session were included in the programme.

The first Annie B. Cuning Lecture on nutrition was given under the auspices of the college in the public lecture theatre of the University of Melbourne on April 8. The lectureship was endowed by Mrs. A. B. Cuning, of Surrey, England, a graduate in Medicine of the University of Melbourne. Colonel C. H. Kellaway, M.C., M.D., M.S., F.R.S., F.R.C.P. (London), F.R.A.C.P., delivered the lecture, which was entitled "The People's Food".

The following new Fellows were elected and admitted at a meeting of the general body of Fellows on April 9: Surgeon Captain W. J. Carr, C.B.E., of Victoria, Director of Naval Medical Services, Royal Australian Navy; Group Captain E. A. Daley, of Victoria, Senior Permanent Medical Officer, Royal Australian Air Force; Dr. Byron L. Stanton, Lecturer in Materia Medica and Pharmacy, University of Melbourne. Major Lucy Bryce, of Victoria, who was elected at the last meeting, was also admitted to Fellowship.

On the recommendation of the Board of Censors, the following candidates who were successful at an examination for membership held prior to the meeting were admitted to membership by the President at the Council meeting held on April 9: Lieutenant Colonel H. R. Love, of Queensland; Dr. Ethel Byrne, of New South Wales; Dr. Margaret M. Henderson, Dr. Henry McLorinan, Major F. H. Moran, M.C., and Dr. Hilary J. Roche, of Victoria; Major J. M. Bonnin, of South Australia; Dr. W. J. Freeman and Dr. James Tremayne, of Tasmania.

The following contributions were given at the scientific session on April 10: Dr. A. B. Corkill: "The Correlation between Experimental Hypertension and Hypertension in Man"; Major William A. Read, United States of America Forces in Australia: "The Cephalin Flocculation Test as an Index of Parenchymatous Liver Damage"; Lieutenant-Colonel J. M. Hayman, 4th United States General Hospital: "Cardiac Output, Blood Volume, Renal Function and other Aspects of the Circulation in Congestive Cardiac Failure and after Recovery".

Discussion followed each of these papers.

## National Emergency Measures.

### NATIONAL SECURITY (MEDICAL COORDINATION EQUIPMENT) REGULATIONS.

#### Amendment of Control of Medical Equipment Order.

THE following is the text of a recently gazetted amendment of the Control of Medical Equipment Order.

In pursuance of regulation 42 of the National Security (Medical Coordination and Equipment) Regulations, I, Samuel Roy Burston, Chairman of the Central Medical Coordination Committee, acting upon the recommendation of the Medical Equipment Control Committee, do hereby order as follows:

After paragraph 9 of the Control of Medical Equipment Order the following paragraph is added:

#### Australian War Pharmacopœia.

"10. (1) In this paragraph 'Australian War Pharmacopœia' means the Australian War Pharmacopœia (1942) compiled and published by direction of the Medical Equipment Control Committee.

(2) Notwithstanding any enactment in force in any State or Territory, when a person is required to supply any medical preparation, on a prescription of a medical practitioner or otherwise, under a title corresponding with a title appearing in the Australian War Pharmacopœia (whether or not any other pharmacopœia is specified in the prescription) he shall supply a preparation dispensed in accordance with the formula in the Australian War Pharmacopœia.

(3) Where the Australian War Pharmacopœia authorises the use of an alternative drug or alternative drugs in any preparation, it shall be lawful for any pharmaceutical chemist to use such alternative drug or drugs when dispensing any prescription for the preparation."

Dated this Fourth day of May, 1943.

(Signed) S. ROY BURSTON,  
Chairman, Central Medical  
Coordination Committee.

As a result of this order, if a medical practitioner desires to order a special prescription, it will be dispensed if he writes the prescription in full. If, on the other hand, he contents himself with writing the name of a stock mixture, the exact composition of the mixture dispensed will be that set out in the Australian War Pharmacopœia.

#### BANDAGE GLUE.

THE following statement is published at the request of the Medical Equipment Control Committee.

Dr. L. J. J. Nye, of Brisbane, in a letter to THE MEDICAL JOURNAL OF AUSTRALIA which was published on August 24, 1940, directed attention to the use of bandage glue as a means whereby economy could be achieved in bandages.

He recommended that every first-aid post should have a bottle of this glue and a brush to apply it, and pointed out that a few turns of a bandage reasonably well stuck by the glue will usually be retained far more effectively than a full bandage applied in the orthodox manner.

At that time the chief need for economy in dressings related to the use of cotton goods, but subsequent developments have made it equally important to adopt every possible means of conserving the use of adhesive tape owing to the fact that rubber is an important raw component of this material.

In view of these facts, the Medical Equipment Control Committee instituted experiments in order to determine the most satisfactory type of glue which might be employed and, further, the technique which should be adopted in the application of the glue. It desires to acknowledge its indebtedness to the Davis Gelatine Company and the first-aid department of the Commonwealth Aircraft Corporation. The technical staff of the company has produced a glue which is now in commercial production under the name of the "Davis Bandage Adhesive". The first-aid department of the factory has supplied information regarding its technical use. This information may be summarized as follows:

1. The glue may be used as a means of fixing a bandage in position. For this purpose, a small quantity is applied to the end of the bandage. As Dr. Nye pointed out, the use of glue in this manner does achieve a material saving in the consumption of bandages.

2. The glue may also be used as a substitute for adhesive tape dressing, particularly in finger injuries. The method adopted is to dress the injury, to apply a small amount of bandage and then to cover the whole of the bandage with glue. This dressing remains oil-proof as long as the surface does not crack, but, of course, is not waterproof. It has been found of considerable benefit in the case of mechanics whose hands are constantly exposed to oil, and workmen who have had a finger dressing of this description express a marked preference for it as it is compact and does not interfere unduly with movement.

"Davis Bandage Adhesive" is being distributed through the usual trade channels in four-ounce and sixteen-ounce jars, and the committee recommends that it should be employed in suitable cases of minor injuries whenever possible in order to achieve economy in the use of both dressings and adhesive tape.

## Correspondence.

### ELECTION OF COUNCIL (ADDENDUM).

SIR: Following discussion of my recent letter on the above, the following points should be added to avoid confusion:

1. I suggest proportional representation so that no small group shall have the same voting power as a large group. This would be done by all members of the British Medical Association being allotted to a group for voting purposes (according to his choice in the first place, failing which, he would simply have his name put in one), and so no member could vote twice. Then a certain membership would be calculated as the minimum required for representation and groups too small would have to combine. I had arbitrarily suggested 80 members per representative.

2. On the question of taking no action while so many doctors are away on service, a decision should be made by postal vote, and if good time were allowed for returns, even six months, there should not be many service members miss out. Further, it would be to the immediate advantage of service members who could have their own direct representative or representatives on the council now by forming a serving medical officers' group. Could that be to their disadvantage? On the other hand, are they likely to approve of us at home letting the grass grow under our feet while they serve? Our fighting colleagues must come back to the best conditions we can make for them, and I submit the above suggestions are basic.

3. Other groups besides local associations would be women's, specialist groups, public service, and resident medical officers, but all would have to meet the membership requirements or combine.

Yours, etc.,

C. C. McKellar.

143, Macquarie Street,  
Sydney,  
March 23, 1943.

### POST-OPERATIVE COLLAPSE AND PULMONARY OEDEMA FOLLOWING LOCAL ANÆSTHETIC FOR RADICAL ANTROSTOMY.

SIR: I am reporting a case of post-operative collapse following local anæsthesia, and the remarkable response to venesection.

Mrs. "A" was operated on in Dubbo Hospital at 9 a.m. for radical antrostomy under local anæsthetic. At 8 a.m., injection a quarter morphia, one one-hundredth hyoscine; second quarter morphia and a hundredth atropine was given 9 a.m. The patient was calm and respiration 20, pulse 100. Operation commenced 9.15 a.m.; 25 cubic centimetres of 1% "Novocain" and 1 in 75,000 adrenaline was used as an infiltration anæsthesia. The nose was packed with gauze soaked in 10% cocaine and adrenaline equal parts. During the operation, the patient became restless; her respiration increased to 50 per minute and pulse was 150 at the end of the operation.

On returning to the ward, she was very cyanosed; the respirations were very shallow—60 per minute. I ordered an injection of "Coramine" and "Carbogen" inhalation, but she gradually became worse and was at death's door during the remainder of the day. At 5 p.m. she developed pulmonary oedema, and after consultation with Dr. Roberts we decided on venesection, and removed one pint of blood. The result was instantaneous, and she made a rapid recovery.

This is the first case I have had of collapse following local anæsthesia. I am reporting this case as it may be of some help to someone who has a similar experience. I think most of the collapse was due to the cocaine.

Yours, etc.,

R. E. BUCKINGHAM.

60, Anson Street,  
Orange,  
New South Wales.  
April 8, 1943.

### THE FUTURE OF MEDICAL PRACTICE.

SIR: It is with great interest that I read the many letters appearing in your journal in reference to the proposed "national medical service".

It amazes me that these discussions continue on, in spite of the altered economical condition of the country today.

Before the war and especially before the "Japs" entered, there may have been a shortage of money, and some difficulty, in certain isolated cases, of people obtaining medical attention through lack of same. Personally I think this state of affairs to have been grossly exaggerated. Today, however, things are different. Never in the history of this country has the working man earned so much money and been able to spend so little. Probably never before has so large a proportion of the medical profession worked for so little. On whose account, then, is it that this scheme continues to be pushed in front of the medical profession?

Let us unhesitatingly declare that no alteration is justified at present, and when the occasion arises, we will deal with it in our own way. The medical profession as a body has proved by its past service that it is aware of its obligations to the country, and can be relied on to continue to fulfil these obligations, both in peace and war, in the future as it has in the past.

Yours, etc.,

R. V. BRETHERTON,

Lieutenant-Colonel.

9 Australian Field Ambulance,  
Australian Imperial Force,  
April 29, 1943.

SIR: Many of our profession appear to accept the fact that a salaried medical service is "just around the corner". Is this an admission of defeat at the hands of our misguided politicians, or acceptance of the "new order" principle? Surely, sufficient evidence has already been produced to prove that no salaried service can ever expect to get the best results from our profession, and even less likely is it to improve the health of our people—which aim must be the underlying motive of any scheme, salaried or otherwise. Ample evidence has also proved that the old order is not so bad. Faults there certainly are, but let us work logically—cut out the dead wood and let the tree live.

Evolution—not revolution! To precipitate any new plan overnight must spell chaos.

Since World War I, note how many reforms have been wrought per medium of three or five year plans—not by hasty overnight changes. But before seeking any change, let us systematically take stock of existing conditions, let us find out exactly what wants changing, next how to change it, and over what period such change should be extended; to forestall any chance of disrupting present machinery that is working smoothly.

Annual complete medical examination has been more than once suggested as a mere part or incident of other schemes. Close inspection surely suggests this, not as a small part of a scheme but as a solid foundation upon which to build. With very little adjustment of our present system we have here a means of securing a complete stocktaking of Australia's health.

Systematically carried out (even if it took two years), it would provide us with invaluable data, somewhere to start. Every person in Australia would have his health card filed at a central bureau, where after examination such cards are checked and graded by medical inspectors, according to type of disability or illness: (a) those requiring immediate attention; (b) to receive attention within three months; (c) pathological peculiarities to be recorded, but not necessarily treated.

By whom and how are such examinations to be carried out? If each practitioner examined several patients daily over the suggested period, this would be accomplished. No patient will be examined by his own doctor, nor shall such patient divulge his own doctor's name to the examiner. An independent report is thus obtained. The patient is notified of results by the central bureau and he returns to his own doctor for treatment.

Inspectors. After being in practice for twenty or thirty years that vast knowledge, laboriously gained by our senior general practitioners, is very often wasted—he slows his tempo with age, retires, and hopes for the best. This is wrong. From this wealth of experience our "inspectors" should be selected and paid a good salary (£2,000 to £3,000) per annum, because, firstly, their experience justifies it, and secondly, the important nature of their work demands it—nor would they require pensions in their declining years. Not only would they report on "health cards", but also reexamine a cross section of patients already seen by general practitioners for their routine "annual". They would have power to suggest, when necessary, that any doctor might benefit himself by a short post-graduate course in whatever

branch he was exhibiting weakness (as shown by repetition of "missed" or wrong diagnoses recorded on health cards). They would also discover in their routine inspection of districts, whether patients were neglecting to report for examination. Also inspect hospitals.

How many tragedies of neglected treatment would and could be avoided by this means? For the very person least able to decide when he should seek treatment is free to make that choice—the layman.

This effort is well worth spending two years upon. The next two years would now be spent (not wasted) in reorganizing hospitals, pathological services *et cetera*, as the survey indicates we would now be in a position to decide precisely what is wanted—what to eliminate. Finally, when this stage is reached, periodical examinations and records will still carry on, but now less effort will be required, because the preliminary ground has been broken and the system working smoothly.

"Free" service may sound tempting to the layman—a catch vote for the politicians—but after all most things that cost nothing are usually worth about the same. A scheme based on the above principles must produce results and it would not throw out of gear our present system of practice, and above all our Treasurer would certainly save many millions when compared with some of our other "all in" or "all out" schemes.

Space permitting, I commend to your attention enclosed article ex *British Medical Journal*, December 12, 1942, which has come to my notice since writing above.<sup>1</sup>

Yours, etc.,

C. R. E. DOWNING,  
75, Anzac Highway, Everard  
Park, South Australia.

Liberal Club Building,  
175, North Terrace,  
Adelaide.  
May 1, 1943.

#### OMISSIONS FROM TEXT-BOOKS.

Sm: In my opinion there are a number of subjects which are inadequately dealt with in the current text-books on obstetrics and gynaecology, the omission of some of which is greatly to the detriment of students and beginners. These are:

1. Antenatal diet—a routine cutting down of meat for every antenatal clinic case from the first attendance of the patient, regardless of whether she has toxic signs and symptoms or not. Meat should be cut down to a maximum of once per day, with a recommendation to cut it down even more than this if the patient is willing to do so. Plenty of fruit and vegetables should be advised.

2. The self-control theory of birth control which in view of recent scientific researches is now much more reliable than formerly and can now be very precisely stated, most dangerous phase of the menstrual cycle being thirteen to fifteen days after the day of onset of menstruation. To be safer, the relatively dangerous phase can also be included, extending the dangerous phase from the ninth to seventeenth days.

3. That the carbon dioxide cylinder is often a life-saving measure in the resuscitation of a newly born babe.

4. That the best way of avoiding a post-partum hæmorrhage is to encourage the mother to push out the third stage herself during contractions, the obstetrician's hand being on the fundus, and the usual prophylactic measures for shock being carried out by the nurse (including hot-water bottles). (A Crêde expression is in most cases avoidable.)

5. That the head in a persistent occipito-posterior position can usually be very easily turned (before applying forceps) if the obstetrician grasps the occiput firmly with his left hand and, while turning the head, also pushes it up somewhat because there is more room in the pelvis higher up where the pelvis is more capacious. The head will slip down lower again by itself after it has been turned. (Even if only half-turned it will be easier to forceps the case than in the persistent occipito-posterior position.)

6. That in view of menstruation, displacement, pregnancy *et cetera*, women should be discouraged from and not forced into hard muscular work and strenuous types of athletics and competitive sport (especially in time of peace). They

<sup>1</sup>The article mentioned is a letter by S. J. Beggs on health centres and periodical medical examination.

are differently constructed from men and should not be regarded as men. (Even men are sometimes physically the worse for strenuous hard work and strenuous competitive sport.) Women should not be advised to bathe and swim during their menstrual periods. Mothers and expectant mothers should not be forced or even encouraged to undertake work outside their own households. I personally hold most emphatic views on these subjects, regardless of modern fashions and also regardless of the views of certain male gynaecological "authorities" and of certain modern political and social "reformers".

7. That the use of rubber contraceptives is extremely likely to greatly increase the incidence of carcinoma of the cervix, as may also certain extraordinary modern mechanical contrivances worn by some women at menstrual periods and constituting an additional type of abomination.

8. That, incredible as it may appear to some types of modern minds, there still remain, even in degraded modern communities, a considerable number of women for whom routine national venereal disease tests are unnecessary—a fact which the profession at least is in a position to appreciate and, from recent newspaper reports, I think that the profession probably does realize this fact. Such women should not be compelled to submit to this degradation and insult. The psychological results of such a procedure may be definitely harmful in many cases.

9. That sterilization operations should be even more safeguarded than they are by necessity for extra consultants (as in the case of an induction curette). The profession should not weakly pander to selfishness, cowardice and vice and should be ready in all cases to bear in mind the serious menace of national extermination.

Yours, etc.,

JESSIE B. SIMPSON.

35, Normanby Street,  
Middle Brighton, S.5,  
Victoria.  
May 12, 1943.

#### Obituary.

BRIAN FORMBY MOORE.

We are indebted to Dr. G. H. B. Black for the following appreciation of the late Dr. Brian Formby Moore.

By the untimely death of Dr. Brian Moore on April 11 the South Australian medical profession loses one of its best known ophthalmologists.

Born in South Australia forty-eight years ago, he secured his earlier education at Saint Peter's College, Adelaide, and was prominent in both academic and athletic spheres.

Commencing his medical studies at the University of Adelaide in 1913, his graduation M.B., B.S. in 1917 was immediately followed by enlistment in the Australian Imperial Force. He served as Captain in the Australian Army Medical Corps in various units on the Western Front in the Great War I until the cessation of hostilities, and was mentioned in dispatches.

On his return to Australia he engaged in general practice at Torrensville. In 1927 he went to England and studied ophthalmology, returning to Adelaide in 1928 to take over the ophthalmic practice of the late Dr. A. M. Morgan. His professional activities since then have been confined to this branch of medicine, only interrupted by a return trip to England in 1935-1936, during which he obtained the D.O.M.S.R.C.P. and S., being already a Fellow of the Royal Australasian College of Surgeons, being elected in September, 1932.

From 1928 until his death he was honorary ophthalmologist to the Adelaide Children's Hospital and he was possibly best known professionally for his work with children. In this connexion, it was by his energy and enthusiasm that orthoptic training was started in South Australia by the formation of the orthoptic clinic at the Children's Hospital.

Since school days he was a keen and successful golfer, and his favourite hobby was woodwork. A number of examples of his cabinet-making skill were shown in the hobbies section at the Australasian Medical Congress in Adelaide in 1937.

Dr. Moore's grandfather, Robert Waters Moore, M.R.C.S., London, 1842, was number 29 of the registered medical practitioners in South Australia (see *THE MEDICAL JOURNAL OF AUSTRALIA*, October 29, 1938) and was Colonial Surgeon from 1858 to 1869.



Brian Moore in 1922 married Miss Joyce Morgan, daughter of the late E. R. Morgan and granddaughter of the late Sir William Morgan. His widow survives him, together with three daughters and one son. The eldest daughter, Anne, is at present serving with the Women's Australian Auxiliary Air Force, the other children being still at school.

#### GUILDFORD MONTGOMERIE DAVIDSON.

We regret to announce the death of Dr. Guildford Montgomery Davidson, which occurred on May 13, 1943, at Sandgate, Queensland.

#### CECIL ROY QUINN.

We regret to announce the death of Dr. Cecil Roy Quinn, which occurred on May 9, 1943, at Caulfield, Victoria.

### Naval, Military and Air Force.

#### CASUALTIES.

ACCORDING to the casualty list received on May 19, 1943, Captain R. W. Greville, A.A.M.C., Hawthorn, who was previously reported missing, is now reported to be a prisoner of war.

### Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Fleming, Justin Paul, M.B., B.S., 1940 (Univ. Sydney), 65, Muston Street, Mosman.

Hirz, Jehuda, M.D., 1934 (Univ. Paris), c.o. Mr. Harris, 51, Moorami Avenue, Kensington. (Registered in New South Wales in accordance with the provisions of Section 17A of the Medical Practitioners Act, 1938-1939.)

### Medical Appointments.

Dr. Hugh Graham Andrew has been appointed to be temporary honorary anaesthetist to the gynaecological section, Royal Adelaide Hospital, Adelaide, South Australia.

Dr. Arthur Charles Savage, pursuant to the provisions of the Health Act, 1935-1941, of South Australia, has been appointed to be an Officer of Health in the areas on and adjacent to the East-West Railway Line from and including Tarcoola to the South Australian border.

Dr. William Thomas Whitby has been appointed Government Medical Officer at Finley, New South Wales.

### Books Received.

"The Forgotten People, and Other Studies in Democracy", by Robert Gordon Menzies; 1943. Sydney and London: Angus and Robertson, Limited. 7½" x 5", pp. 202. Price: 4s. 6d.

"Coast to Coast: Australian Stories, 1942", selected by Beatrice Davis; 1943. Sydney and London: Angus and Robertson, Limited. 7½" x 5", pp. 247. Price: 7s. 6d.

"Electrocardiograms: An Elementary Atlas for Students and Practitioners", by H. Wallace Jones, M.D., M.Sc., F.R.C.P., and E. Noble Chamberlain, M.D., M.Sc., F.R.C.P.; Second Edition; 1943. Bristol: John Wright and Sons, Limited; London: Simpkin Marshall (1941), Limited. 8½" x 5½", pp. 56, with 53 illustrations. Price: 5s. net.

"Fractures and Fracture Treatment in Practice", by Kurt Colsen, M.D.; 1942. Johannesburg: Witwatersrand University Press. 8½" x 5½", pp. 157, with 157 illustrations. Price: 12s. 6d.

### Diary for the Month.

- JUNE 1.—New South Wales Branch, B.M.A.: Organization and Science Committee.  
 JUNE 2.—Victorian Branch, B.M.A.: Branch.  
 JUNE 2.—Western Australian Branch, B.M.A.: Council.  
 JUNE 3.—New South Wales Branch, B.M.A.: Special Groups Committee.  
 JUNE 3.—South Australian Branch, B.M.A.: Council.  
 JUNE 4.—Queensland Branch, B.M.A.: Branch (Joseph Bancroft Memorial Lecture).  
 JUNE 8.—New South Wales Branch, B.M.A.: Executive and Finance Committee.  
 JUNE 8.—Tasmanian Branch, B.M.A.: Branch.  
 JUNE 11.—Queensland Branch, B.M.A.: Council.  
 JUNE 15.—New South Wales Branch, B.M.A.: Ethics Committee.  
 JUNE 16.—Western Australian Branch, B.M.A.: Branch.  
 JUNE 17.—New South Wales Branch, B.M.A.: Clinical Meeting.  
 JUNE 22.—New South Wales Branch, B.M.A.: Medical Politics Committee.  
 JUNE 23.—Victorian Branch, B.M.A.: Council.  
 JUNE 24.—New South Wales Branch, B.M.A.: Branch.  
 JUNE 24.—South Australian Branch, B.M.A.: Branch.  
 JUNE 25.—Queensland Branch, B.M.A.: Council.

### Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmalm United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phoenix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia.

### Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

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Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility unless such a notification is received within one month.

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